ENCAPSULATING PERITONEAL SCLEROSIS: CLINICAL INSIGHTS AND TREATMENTS OPTIONS
Martin Wilkie, Sheffield, UK

Chair: Simon Davies, Stoke-on-Trent, UK
Nicholas Topley, Cardiff, UK

Prof Martin Wilkie
Sheffield Kidney Institute
Sorby Renal Unit
Northern General Hospital
Sheffield, United Kingdom

Slide 1
Encapsulating peritoneal sclerosis – clinical insights and treatment options

Dr Martin Wilkie
Reader in medicine
Sheffield Kidney Institute

... for giving me the opportunity to talk about encapsulating peritoneal sclerosis. So I’m going to discuss a bit about the clinical insights, that’s kind of assuming that I have any clinical insights but I have some. I’ve been in this area for probably 20 years so I have been exposed to these cases and have read the literature to some extent. So I’m going to share that with you.

I’m going to talk a bit about treatment options although the information on treatment options isn’t very robust and I think the message I’m going to give you is that it’s really important that we’re frank about the difficulties we have both with our ability to screen for this condition, our ability to diagnose it clearly and in a robust fashion and our ability to understand the treatments.

Listening to some of the presentations we’ve had so far during this meeting there are lots of areas of uncertainty in our practice and it seems to me as I grow older that as uncertainty grows, it really is important that we give our patients a greater opportunity to be engaged in that discussion and in decision making because they have an opinion even if there’s considerable uncertainty.
Paul

- A 45-year-old man with end-stage renal failure presented with peritonitis and a painful ischemic right leg following routine hemodialysis in June 2009.
- Sensation, motor function, and pulses below the femoral artery in the right leg were all absent; duplex scanning revealed no audible Doppler signal.
- He had no prior symptoms suggestive of impending EPS.
- His medical history included 6 years of PD prior to conversion to hemodialysis, which was undertaken because of concerns about developing EPS through long-term PD (although there were no suggestive symptoms at the time).

Kirkman MA et al, PDI 2010.

So, that’s a little bit of an introduction and we’ll start off with a patient, Paul and his case is published in PDI. So if you’re case has been published in PDI, it’s probably not a good thing from the point of view of your general condition. You’ve probably got a significant medical problem of some sort.

Paul a 45 year old man presented with ESRD, with peritonitis and an ischemic leg following a routine hemodialysis session. On physical examination it was clear that the leg was ischemic, there were absent pulses and indeed he underwent a left right fem-pop bypass in order to re-establish perfusion in the leg. He’d had no prior symptoms suggesting EPS but he did have 6 years of PD converted a year previously to HD, to hemodialysis because of concerns that he might develop EPS. In fact, we spent quite a lot of time talking to him about that and trying to engage with him in discussion. Interestingly, he’d had a malignant melanoma in the years gone by which is why he wasn’t on the transplant list. So his competitive risks were already getting complicated and that kind of issue does need to be considered as we try to take that further forward.
So on laparotomy and he was transferred to Manchester under the care of Titus Augustine who operated on him and he found that he had EPS with cocooning and he went on to do both a peritonectomy and also an enterolysis and he removed a lot of ischemic small bowel and he found a large abscess in the sub hepatic area and left him with a metre of bowel and a fistula and also a stoma. He had a long period of in-patient stay and is now not on PD but on parenteral nutrition and on HD. In fact, he’s physically well and playing football if that’s an important marker of physical wellness. Also he’s being considered to go back on the renal transplant waiting list.
What does this case show us?

- EPS tends to affect younger people with low co-morbidity.
- Elective discontinuation of PD was not preventative.
- The presentation was unexpected 1 year post PD
- The combination of surgery & TPN were lifesaving

So what does this case tell us then? I’m being philosophical because I don’t really have data but the first thing I think, despite what Simon showed us from the Australian data, is that EPS tends to affect younger people with low co-morbidity and the reason why it does that of course is you have to live long enough to get EPS. If you’re a high risk individual who’s going to die of some other event beforehand, then you’re less likely to get EPS.

The second thing is patently in this particular case and clearly we’ve a lot to learn about risk management discontinuing PD wasn’t preventative.

Thirdly, a presentation was unexpected and in other words we weren’t very good at making his diagnosis, screening for his diagnosis, anticipating it and coming up with pre-emptive therapy. It came as a bolt from the blue.

Finally and I don’t think we can contest this, in his particular case surgery and parenteral nutrition were lifesaving.

Slide 5
So that’s by way of an introduction. I turn now to the Scottish study which Simon told us a bit about and you can see the survival curves of those who got EPS versus those who didn’t and I think the thing about that study and I think the Scottish team have pointed this out that in their experience EPS adversely affected the outcome for those patients with otherwise excellent prognosis. So that’s where there is a slight difference with the Australian experience I think. You can see that survival curve if I show you at the top there the patients who were going to get EPS clearly had to survive getting EPS. So it did identify possibly a group who were younger and who had low co-morbidity before they then got this linear decline which we can see on the red line there. So that is an interesting observation.

Could we have screened him for EPS? Well, we couldn’t really.

Slide 7

CT scan scores of prediagnostic scans taken more than 4 mo before diagnosis, compared with CT scans taken at the time of diagnosis of EPS.


This is data from Ruth Tarzi working with Edwina Brown and others showing the development of a screening score for EPS based on a number of different factors including membrane thickening, calcification, tethering of small bowel and a variety of
other factors which they validated and it’s a robust score for diagnosing EPS but when they looked at the scans in which they made the diagnosis if the patients had had a previous scan, they found out actually that they didn’t have significant scores beforehand. So in other words, this condition wasn’t visible on the CT scan pre-emptively. Screening wasn’t a particularly useful test in their experience with CT scanning that is.

Slide 8

Disruption of the “slide and glide”

Are there other techniques that we can use? We’ve been interested in this video MRI and I can show you on the left a video MRI loop of somebody with a normal abdomen and on the right somebody in this case with an adhesion.

This is from work from Rotherham. You’ll know Rotherham it’s got a football club. Anyone heard about Rotherham football club? No, OK someone at the back has that’s good.

So, this is a group that are already working with this video MRI concept and I think it’s really interesting because once you’ve seen video MRI, you think to yourself well why do we look at static images? Clearly it would be a bit like looking at static echocardiograms or something of that sort.

Slide 9
So there’s potentially a lot of information to come from video MRI. Of course, we don’t know yet whether it’s relevant and the mathematics in terms of its analyses are really complicated because it requires complex vector analysis and mathematical modelling. Here are a couple of cases that were Manchester patients who were about to go to surgery and you can see in panel 2 and 4 you can see all of the movement in the EPS patients is confined to a very small area in the abdomen, certainly at the top of the abdomen and there’s sort of a piston effect. Whereas, in the normal cases on the left you can see movement distributed throughout the whole of the abdomen and of course, the peritoneal membrane is responsible for allowing the slide and glide of intraperitoneal contents, so possibly with time and good grant money it should be possible to use this technique maybe as a screening tool but as yet we don’t have a screening tool for people who might be about to develop EPS. So more work to be done there.
Should we have switched him from PD because of concerns about EPS?

Now, this question’s already been addressed and I’m going to go through a couple of slides rather quickly because they show what Simon has shown already but I perhaps will bring a slightly different clinical perspective.

Slide 11

NICE Clinical Guideline 125 2011

- Do not routinely switch patients on PD to a different treatment modality in anticipation of potential future complications such as EPS.
- However, health care professionals should monitor risk factors such as loss of UF and discuss with patients regularly the efficacy of all aspects of their treatment.

Should we switch patients? Well we’ve just had nice clinical guideline 125 and there you are and I’ve quoted from nice clinical guideline 125, are you all aware of the
National Institute of Clinical Excellence? They do a very good literature review and I think that’s really a robust component of the work that they do.

But they suggested based on reviewing the literature that one shouldn’t routinely switch patients on PD to a different treatment modality in anticipation of potential future complications such as EPS. So they’re quite clear about that. However, at the same time they suggested that health care professionals should monitor risk factors in terms of planning their care. So we have to sort of balance both of these things and Simon has already shown us evidence for that and indeed the ISPD wrote a guideline in 2009 that was very similar telling us that we should really consider our patients as individuals and make individual decisions. That’s quite difficult.

Slide 12

**EPS incidence varies across the world**

![Graph showing EPS incidence across different regions and countries]

Habib et al Netherlands Journal Of Medicine 2011

We’ve already seen the data on the associated risk factors. I’m going to flick through them very quickly because I don’t think there’s any point in showing you them again except I really like this graph which was produced by the people from the Netherlands and it’s a really nice graph because it puts together for the first time the risks according to the different studies of EPS and you can see looking at that graph a cumulative incidence of 2.1% at 5 years in Japan, whereas 8.1% in Scotland. So clearly big variations across the world and that is very important because that suggests there are variations in the clinical practice which feed into this too. Of course, the data from the paediatric studies is even lower than that 2.1%.
So I’m flicking through these quickly,

Risk factors associated with EPS – from the Dutch EPS study

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate Odds ratio</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of PD</td>
<td>1.49&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age at PD start</td>
<td>0.97&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Transplantation (Tx)</td>
<td>4.63&lt;sup&gt;c&lt;/sup&gt;</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time to EPS from last Tx&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.93&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Calendar time&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1.28&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of icodextrin use</td>
<td>1.92&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ultrafiltration failure</td>
<td>4.55&lt;sup&gt;c&lt;/sup&gt;</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of follow-up&lt;sup&gt;f&lt;/sup&gt;</td>
<td>1.07&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.001</td>
</tr>
<tr>
<td>Transfer to HD from PD for other than suspected EPS</td>
<td>0.98</td>
<td>0.1</td>
</tr>
<tr>
<td>Peritonitis episodes</td>
<td>1.05</td>
<td>0.110</td>
</tr>
</tbody>
</table>


Korte M et al Perit Dial Int 2011; 31(3):269-278
you’ve seen that already

Slide 15

The potential role of risk factor analysis in decision making – hypothetical patients on PD for 5 yrs

<table>
<thead>
<tr>
<th>Factor</th>
<th>Case 1</th>
<th>Case 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>Glucose exposure in last 12 months</td>
<td>1.36%</td>
<td>1.36 / 2.27%</td>
</tr>
<tr>
<td>Icodextrin use (ever)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Dialysis dose</td>
<td>8l</td>
<td>14l</td>
</tr>
<tr>
<td>Residual renal function</td>
<td>20l Cl per week</td>
<td>anuric</td>
</tr>
<tr>
<td>Ultrafiltration capacity</td>
<td>250 ml</td>
<td>150 ml</td>
</tr>
<tr>
<td>Peritonitis episodes</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Co-morbidity</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Transplant listing status</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>Vascular access status</td>
<td>difficult</td>
<td>no</td>
</tr>
<tr>
<td>Patient preference</td>
<td>Clear preference to remain on PD</td>
<td>Flexible</td>
</tr>
<tr>
<td>Possible decision re outcome</td>
<td>Remain on chosen therapy</td>
<td>Planned transfer to HD (home HD?)</td>
</tr>
</tbody>
</table>

but I put together this table just trying to think about it myself. So here we have two different cases and it’s a sort of situation that you would confront trying to decide with your patient should one go ahead and arrange pre-emptive transfer or not? This is a question that we all wrestle with on a regular basis and we discuss this at our weekly multidisciplinary team meeting reviewing data etc. and try to come to a decision and I must say it’s really challenging. In these two cases what I’ve done is I’ve tried to polarise them as being very different to each other. So I’ve given you somebody here who is quite elderly, who’s got some residual renal function, who has reasonable ultrafiltration capacity for example, and for whom vascular access would be difficult because as our previous questions have suggested what you swap to is clearly very important. Geoff Pearl showed us recently from the Canadian registry that if you dialyse in a line and many other studies have shown this that your outcome is less good and clearly that’s part of the balance in terms of competitive risk. On the right hand panel case 2 I give you someone who is younger, who’s anuric, who has lost ultrafiltration capacity and you know who’s uncertain about their preference perhaps and who’s on the transplant list. So these are very different individuals. I think it’s only the sort of study that’s Simon talking about that is going to help us resolve these and help us make a decision.
One of the things we sometimes do is we give people a trial of hemodialysis because some people will say ‘well I’ve tried that hemodialysis and I don’t really get on with it very well and I’d like to come back to peritoneal dialysis thank you, even though I’m aware that there’s a risk associated with this particular treatment’.

I’m going to go through this very quickly because you’re not meant to see those, so you haven’t.
So what about making the diagnosis? I told you about Paul at the beginning we weren’t very good at making his diagnosis. How should we be making the diagnosis?

Diagnostic criteria for EPS used in the NEXT-PD study

- **Stage 1**: Increase in non-inflammatory ascites
- **Stage 2**: Increase in inflammatory ascites (increased leucocytes in ascites), general inflammatory reaction
- **Stage 3**: Increase in inflammatory ascites and bowel obstruction symptoms
- **Stage 4**: Continuous or severe bowel obstruction symptoms

Well, our Japanese colleagues have set up a prospective study in the biocompatible era looking at a cohort study of EPS. So they called it the next PD study. They’re using a fairly clear diagnostic classification there and I’ve put it on the slide dividing EPS into various stages: increases in non-inflammatory ascites, presumably for people who’ve come off PD and are on hemodialysis, inflammatory ascites and then bowel obstruction and then continuous or severe bowel obstruction symptoms. So that’s interesting, that looks straightforward. The trouble with it is it’s really difficult to apply.

I’m going to use some of the slides from Helen Hurst’s PhD thesis in the next part of my talk. Helen Hurst who’s just been awarded her PhD at Manchester has been interviewing patients who have experienced EPS and who have been operated on, survivors not all of them are still survivors and asked them what it’s like. I think that’s a really challenging piece of work and gives us some really important information from the patient perspective. If we look at it differently to the next PD approach, the difficulty is that we’ve got a patient on PD who’s then developing a range of vague symptoms and we really have difficulty picking that up.

So, I think one of the key messages is that we’re not very good at identifying the diagnosis or perhaps giving our patients information about it so that they can help us in that discussion.
There are a whole range of symptoms that patients might experience and if you look at them they’re documented on this slide from one of the studies from Manchester. But those symptoms again may be vague and we may not be very good at picking them up and clearly it’s important that we are better educated, particularly in people who have come off PD and are now on HD and they’re HD satellite unit somewhere that we’re perhaps more on to the symptoms.

Slide 21

**GI symptoms 6 months pre-diagnosis (black bars) and at time of diagnosis (hatched bars) with EPS.**

De Freitas et al, Perit Dial Int 2008; 28:271–276
So this is from Helen’s thesis and she’s done some qualitative interviewing as I said to sort of understand the experience that these patients have had. In the top circle there is some stuff here about understanding EPS, what it feels like and when I asked Helen is there one message that I ought to share with the good people at the EDTA from your thesis? She said to me the key message is this business about not being heard and patients experiencing symptoms and saying there’s something wrong with me doctor but their doctor is not really being able to understand it and make the diagnosis. So that clearly is very important and that feeds into the information about knowledge and information gaps and of course, for the patient the shock that they’ve got such a serious condition.

On the right here we’ve got some of the information about the experience of EPS, the need to endure because if you look at these inpatient stays that many of these patients experience, they’re several months and then of course, the impact on the body in terms of for example, stomas, nutrition and struggles with eating.

Then on the left hand side we’ve got some information about the journey and support.

Slide 22

‘Not being heard’

- “I had been saying for a year surely there’s something some one can do ..I can’t keep suffering..it was horrendous the pain was getting worse.”

- P: Yeah. I get quite surprised when people say things to me, you know, like ‘We didn’t think you were coming back’ and stuff. And lots of people had said that.

- I: What did it make you think when they said it? What did you feel?
- P: I was a bit taken aback because nobody said anything at the time. You know, they didn’t... they didn’t even register that I was in pain really, at the time. Because they couldn’t do anything about it – nobody could do anything. And I used to feel quite upset because I was rolling around in pain and crying and screaming and they would be over the other side of the ward telling jokes and things, you know?

Helen Hurst PhD thesis

So these are some of the themes that have come out of her work and here’s one slide that she gave me dealing with this issue of not being heard. I think it is worth just reviewing this. These are quotations from her interviews. Patients saying that ‘I had been saying for a year surely there’s something one can do, I can’t keep suffering. It
was horrendous. The pain was getting worse’. So these kinds of themes that she finds from speaking to people who have subsequently been diagnosed of suffering with EPS.

I get surprised when people say things to me you know like we didn’t think you were coming back and stuff and lots of people have said that. I was a bit taken aback because nobody said anything at the time you know, they didn’t even register that I was in pain really at the time because they couldn’t do anything about it and of course, helplessness from the doctor’s sort of feeds into that kind of atmosphere.

Slide 23

**Implications and Recommendations**

- **Early symptom recognition**
  - Consider written information/access to early symptoms for PD patients
  - Improve knowledge and skills within HD units to inform and detect early signs
- **Information needs**
  - Preparing patients for the impact and longevity of recovery
  - To continue to consider ways we discuss the risks of PD in particular preparation for transitions to HD
- **Support**
  - Cost of travel/family support
  - Networks

Helen Hurst PhD thesis

Her summary really is focused around the importance of early symptom recognition and sharing information with patients so that they can work with us on that I think to try to enhance diagnosis at least so that patients don’t have that feeling of isolation that they get when they know they’ve got a condition but their physicians aren’t really able to pick it up.

Slide 24
So what about therapeutic strategies?

Slide 25

The stages of progressive EPS with suggested treatment.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Suggested Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-EPS (1)</td>
<td>Peritoneal rest</td>
</tr>
<tr>
<td>Inflammatory (2)</td>
<td>Corticosteroids – consensus lacking regarding indication, dose and duration.</td>
</tr>
<tr>
<td>Encapsulating (3)</td>
<td>TPN – poor outcome as sole therapy, recommended as adjunctive to other therapies Tarnoxifen.</td>
</tr>
<tr>
<td>Bowel obstruction (4)</td>
<td>Total intestinal enterolysis – recent data suggests that the surgical technique is of major importance.</td>
</tr>
</tbody>
</table>


Again I turn to the Japanese experience. Kawanishi published in PDI a strategy based around the different stages of EPS as he saw it from the Japanese perspective and the kinds of treatment. Now again, we have difficulty in Europe because we don’t really understand what pre-EPS means. Clearly if we knew at the right stage, if we could
understand what that was, then we would know that the time had come to go for peritoneal rest but I don’t think we’re in that position yet.

They hypothesized it with an inflammatory phase when I ought to use perhaps corticosteroids and later on TPN with tamoxifen and then surgery.

Slide 26

**Series describing treatment for EPS**

15 cases - overall survival 60%
- With TPN alone remission was 33%
- Steroids did not improve survival
- With surgery mortality was 33%


<table>
<thead>
<tr>
<th>Therapy</th>
<th>Patients</th>
<th>Recovery (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TPN only</td>
<td>3</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>39</td>
<td>15 (38.50)</td>
</tr>
<tr>
<td>SURGERY</td>
<td>12</td>
<td>7 (58.3)</td>
</tr>
</tbody>
</table>

Kawanishi H et al AJKD, 2004:44(4); pp 729-737

But of course, the evidence behind this is not robust and indeed these are the sorts of studies that were drawn into that sort of information. You can see in the top study 15 cases with 40% mortality. In the lower study again about 50 odd cases with a similar mortality. So clearly the difficulty with this disease is that it is rare, very difficult to study and the information is anecdotal.

Slide 27
I think this paper that was published last year from the Dutch group is really helpful. Again it’s a retrospective study of 63 patients who they looked at between I think 1997 through to 2005 that sort of era, who had had EPS and looked to see what kind of therapies they’d had and interestingly the presence of tamoxifen as a therapy did have a significant impact on survival moving patients from a survival of 46% up to about 74%. So there was a significant impact of tamoxifen although there was no impact in that study of corticosteroid therapy. Clearly that’s a retrospective study but it’s very, very difficult to study this condition prospectively because of its rarity and we may never be able to do so.

Slide 28
Nicola Braun from Stuttgart has been looking at various components of the EPS histology and looked at the oestrogen presence of oestrogen receptors showing that there is a real perhaps absence of oestrogen receptors interestingly because tamoxifen interacts with oestrogen receptor but it also inhibits TGFβ-1 production. So I think more interest there from the histopathology that may be helpful to us.

What about the paediatric data? I’m very grateful to the paediatric team for sharing this with me. This is unpublished data from Rukshana Shroff and others and you can see from the paediatric dialysis working group 1381 patients, children who had received PD over 10 years in 12 European countries and from that group 24 cases of EPS have been identified which gives you a prevalence of 0.17 cases per patient per year which is really pretty low, much lower than in the adult population.

Again, they show you the outcome data there with 2 deaths. I think speaking to Constantinos Stefanidis, he told me that he thought that the outcome in the paediatric population was probably better than in the adult population and that perhaps they behave differently but we don’t know absolutely for sure.

Slide 29
So what about nutritional support?

This data is from Nevine El-Sherbini and has been submitted for publication. She works with Edwina Brown at the Hammersmith hospital. They looked at 15 patients whom they treated with parenteral nutrition and you can see in the top panel the 12 that required parenteral nutrition and she tried to score these using various scores including subject to global assessment and GI symptom scores and that sort of thing.

From her group of 15 patients 5 died so again it’s a similar sort of mortality of a third and some of them were able to come off parenteral nutrition, others remained on parenteral nutrition going forward. She tried to look at which factors really influenced outcome. If you look at both of these groups the poor outcome is on the right.
These are the ones who didn’t survive or remained on long-term parenteral nutrition compared to those with the favourable outcome and interestingly, looking at the risk factors it’s really hard to separate between these tow groups at baseline. The only real difference there was the CRP. I mean there were some differences which are perhaps approaching significance if there was a larger study. For example, presence of GI symptoms or nutrition scores but in that study they’re not really giving us a clear signal as to who’s going to do well and who’s going to do badly and in particular trying to help us decide who would do better on parenteral nutrition and who ought to be referred to surgery and we just don’t know that answer.

Slide 31
High risk of developing refeeding problems if -

- one or more of the following:
  - BMI less than 16 kg/m2
  - unintentional weight loss greater than 15% within the last 3–6 months
  - little or no nutritional intake for more than 10 days
  - low levels of potassium, phosphate or magnesium prior to feeding.

- two or more of the following:
  - BMI less than 18.5 kg/m2
  - unintentional weight loss greater than 10% within the last 3–6 months
  - little or no nutritional intake for more than 5 days
  - a history of alcohol abuse or drugs including insulin, chemotherapy, antacids or diuretics.

From NICE clinical guideline 32
Jordaan A et al PDI. 2007 Jan-Feb;27(1):100-1

It is important to draw attention to the re-feeding syndrome which can occur when malnourished patients receive parenteral nutrition. That’s important to bear in mind. It’s associated to hypophosphatemia, rhabdomyolysis and respiratory and cardiac problems and one needs to be aware of that.

Slide 32

The role of surgery in EPS

So what about the role of surgery?

Slide 33
I was very pleased to receive this data from Titus Augustine at about 1.20 am yesterday. He really sort of made a real effort to get his data together so that we could have a little look at it together and I’m really pleased to be able to share it with you.

So he’s operating at Manchester Royal Infirmary on patients referred there with EPS and has been doing so for some years. He did separate out the data from the last 3 years in which the outcome is slightly better but I thought I’d just show the whole period.

So during that period of time 143 patients proceeded to surgery and you can see the sex distribution there. 28 of those were post-transplant cases. You can see the overall mortality was again a third. It’s interestingly a common theme in these studies whether it’s parenteral nutrition or whether it’s surgery or in most of the other studies mortality seems to be in this sort of range.

Interestingly the post-transplant EPS mortality did seem to be lower than the non-transplant population. I think the other message which is really important from Titus’s work and from the work of that team is that patients who were operated as an emergency had twice the mortality of those who presented semi-electively.

So it’s really a challenge when thinking about surgery in these patients that they need to be referred in a timely fashion so that they can be operated on in a timely fashion.
Patients alive (100) (69.9 %)

- 4 Paediatric (All alive after enterolysis)
- 15 patients transplanted after Enterolysis and Peritonectomy
- 13 Kidneys and 2 Simultaneous Pancreas and Kidneys
Several patients currently being worked up for transplantation
3 patients have supplemental PN
1 being evaluated for kidney and bowel transplantation (short gut after resection for EPS related bowel ischemia)

**RECURRENTCE**

- 16 Cases
- Majority within 24 mths
- Longest at 8 yrs (Mortality)
- 13 Re-operated (3 3 times)
- Mortality 4 (25%)

Titus Augustine, personal communication

So these are the patients who are still alive from his experience, 100 patients still alive and I’ve listed them there. 15 have received renal transplantation after enterolysis and peritonectomy. There’s one being worked up for bowel transplantation and you can see some of the paediatric cases there. Another question which is often asked is recurrence and we’ve seen recurrence in 16 cases and quite a lot of operations required in that group with the longest at 8 years.

**Surgery for EPS**

- Admission
- TPN line
- Feeding and dialysis
- Surgery – Laparotomy and Enterolysis with delayed closure of abdomen with a biologic mesh. Seems to get the best results.

Titus Augustine, personal communication
So that gives you some of the information from the Manchester experience. I wanted to compare that before we do that this is his protocol if you like. All these patients received parenteral nutrition to try to optimize them pre-operatively and they performed enterolysis and they performed a delayed closure of the abdomen with a biological mesh which you can see in the lowest image there. That’s the biological mesh. This looks at the material that they take out, the horrible inflamed sort of fibrin-like material, which is presumably responsible for that elevated CRP that these patients have. In the top panel you can see the cocoon in one of the cases that he operated on.

**Seventeen years' experience of surgical options for encapsulating peritoneal sclerosis**

239 enterolysis procedures in 181 patients over 17 years

**Median survival after diagnosis**
- death from any cause 43.9 months
- death from EPS 35.7 months

<table>
<thead>
<tr>
<th>Years post surgery</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>5</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>% overall survival</td>
<td>93</td>
<td>83</td>
<td>78</td>
<td>71</td>
<td>60</td>
</tr>
</tbody>
</table>


So to compare this with the Japanese data recently I obtained this from an abstract. I haven’t seen the full paper but really some remarkable survival data from the Japanese experience. I don’t think the Manchester survival data is approaching that but I think we can see from both of these experiences that surgery, particularly pre-emptive surgery, does provide at least a respectable treatment that we can offer these patients.

So I want to summarise by saying when we look at this complex condition, I think it’s important that we really recognise how little we know about it. We’re unable to screen for it effectively. We have difficulty making the diagnosis and it’s really important that we are aware of that because some of our patients who experience this condition feel isolated when they know that there’s something wrong with them and their doctors aren’t picking up on it.
Last word

“When they said to me, ‘Oh you could get EPS and it’s horrible,’ and I thought, well I’ll be the one that don’t get it. But I was on PD for 12 ½ years and that suited me. I mean I’d have done another 12 ½ on it if I could........ I hate haemodialysis, it don’t suit me at all. I don’t like it. And if I could have an artificial peritoneum put in I would go back on CAPD, definitely, I would.”

Helen Hurst PhD thesis

We’re not good at identifying the treatment and that all feeds into the need for the sort of prospective studies that Simon has been talking about. I want to leave you with one of Helen’s patients just to show you how resilient and robust our patients are. They’re really remarkable individuals. This person says when they said to me ‘Oh you could get EPS and it’s horrible and I thought well I’ll be the one that doesn’t get it but I was on PD for 12 and a half years and that suited me. I’d have done another 12 and a half on it if I could have. I hate HD, it doesn’t suit me at all, I don’t’ like it. If I could have an artificial peritoneum I’d go back on CAPD I definitely could’. So there’s a patient who’s had EPS, who’s been operated on and is now on HD and who says if you can give me another peritoneal membrane I’ll go back on CAPD.

So thanks for your attention. I hope that my insights were of use.