G9 Encapsulating Peritoneal Sclerosis in Scotland

Introduction

Encapsulating peritoneal sclerosis (EPS) is a devastating complication of peritoneal dialysis (PD), first described in 1980[1]. It is thought to result from chronic intra-abdominal inflammation which is multi-factorial in origin. Length of PD exposure represents the most consistent risk factor identified[2-6].

EPS is uncommon, but the exact incidence is unknown. Multi-centre studies in Japan report rates of 0.8-2.5% of PD patients[2,3,5,6]. A recent UK case series identified 27 EPS cases, indicating a rate of 3.3% over 7 years[7]. An earlier Australian study identified 54 cases in 14 years, giving a rate of 0.7%[4].

The clinical features of EPS have been described previously. Onset may occur on PD, but most cases become apparent after stopping PD, including after renal transplantation[2-8]. The clinical, radiological and pathological criteria for EPS diagnosis were defined by the International Society for Peritoneal Dialysis (ISPD) in 2000[9].

There is little evidence to guide management of EPS patients and there are no reliable biochemical or radiological screening tests that identify patients at risk of, or in the early stages of EPS[10,11].

Aims

The primary aim of this study was to report the incidence of EPS in patients using PD for established renal failure in Scotland between 01 January 2000 and 31 December 2007. A secondary aim was to characterise these cases.

Methods

All patients treated at an adult renal unit who started PD between 01 January 2000 and 31 December 2007 in Scotland (n=1238) were identified from the SRR. The 10 adult renal units in Scotland were asked to identify potential EPS cases diagnosed on or after 01 January 2000. Medical records were examined to ensure all cases met ISPD diagnostic criteria including the presence of typical clinical features and confirmation by radiology or histopathology examination[10]. Exclusion criteria were adhesions attributable to another cause or an alternative explanation for the clinical presentation. Seven patients were excluded because there was another potential cause for their presentation (n=5) or they lacked radiological or pathological confirmation of EPS (n=2). An episode of peritonitis was defined as a PD effluent white cell count above 100 per mm^3 with more than 50% polymorphonuclear leucocytes.

We also looked for missed cases by checking the SRR linked ISD database of in hospital discharge statistics for appropriate ICD-9 or ICD-10 codes. No additional cases were found. All cases have been used to describe the clinical presentation. Only the patients who started PD after 01 January 2000 are used to calculate the incidence of EPS. For clarity we refer to the 46 period-prevalent cases as Group A and the sub-group of 19 incident cases as Group B.

The incidence of EPS was calculated as the number of EPS cases divided by the number of patients at risk, taking into account the person-time during which events were observed as well as the time elapsed before EPS was diagnosed. Logistic analysis was undertaken and odds ratios calculated to compare length of PD exposure and probability of developing EPS. Cumulative risks were calculated using the Kaplan-Meier method to plot the time from first PD exposure to the EPS diagnosis. Peritonitis rates were calculated as the number of patient months on PD divided by the number of infections and expressed as number of months between episodes. Rates were converted to events per person-years for Poisson regression analysis to test the difference between the groups (relative risk).

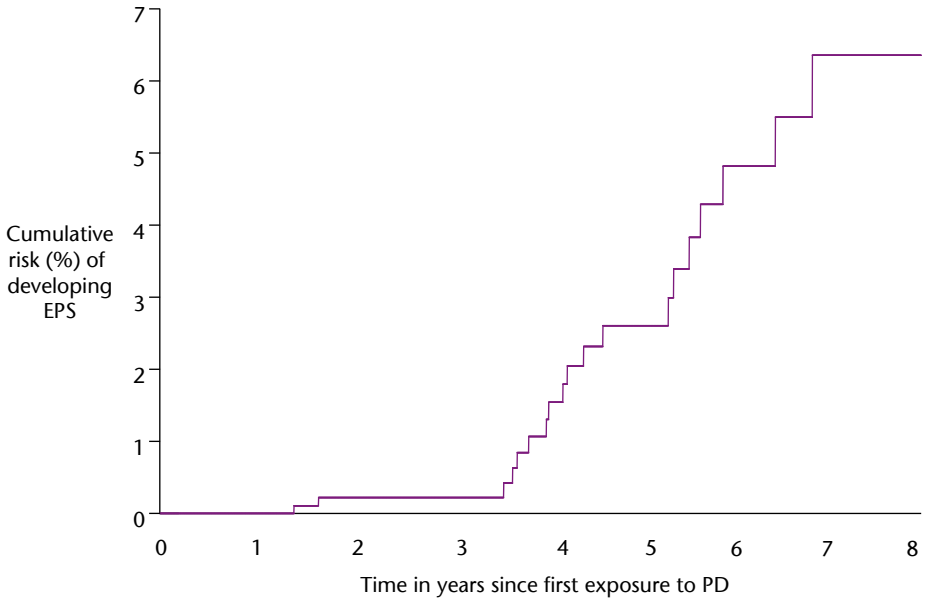
Results

G9.1 Rate of EPS according to duration of PD exposure

PD Exposure (years)	PD patients at risk (n)	EPS cases (n)	Incidence (%)	95% confidence intervals
<1	480	0	0	-
1-2	326	2	0.6	0.2 – 2.1
>2-3	202	4	2.0	0.8 – 5.0
>3-4	114	4	3.5	1.4 – 8.7
>4-5	62	5	8.1	3.6 – 17.6
>5-6	34	3	8.8	3.2 – 23.1
>6	20	1	5.0	1.2 – 23.8
Total	**1238**	**19**		

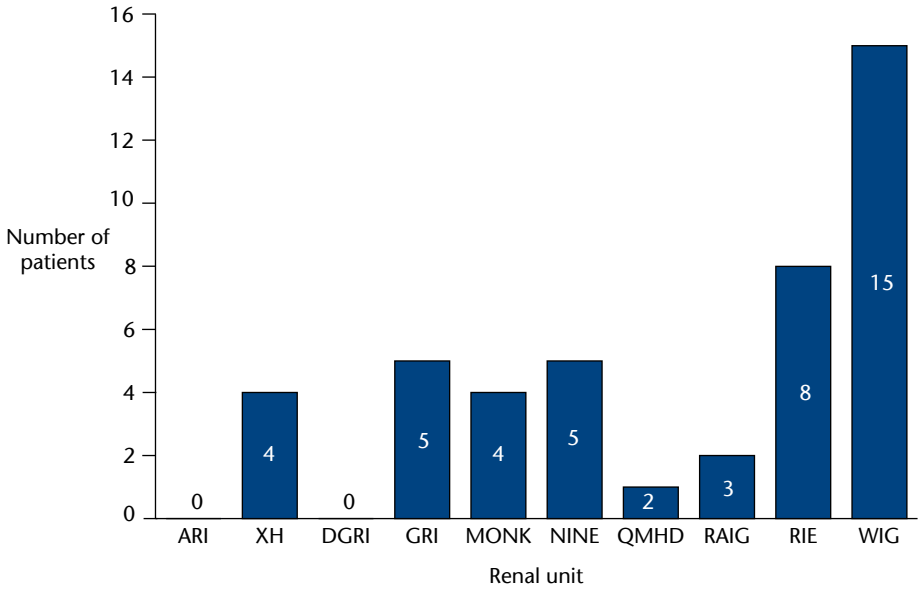
Between 01 January 2000 and 31 December 2007, 46 patients met ISPD diagnostic criteria for EPS (Group A), of whom 19 were first exposed to PD on or after 01 January 2000 (Group B). Of the 1238 patients exposed to PD after 01 January 2000, the overall rate is 1.5% in the 8 years to end December 2007 (19/1238). This amounts to an incidence of 4.9 per 1000 person years or 8.7 per 1000 person years of PD therapy.

G9.2 Cumulative risk of developing EPS from day 1 on PD therapy (censored for death but not change in modality of renal replacement therapy)



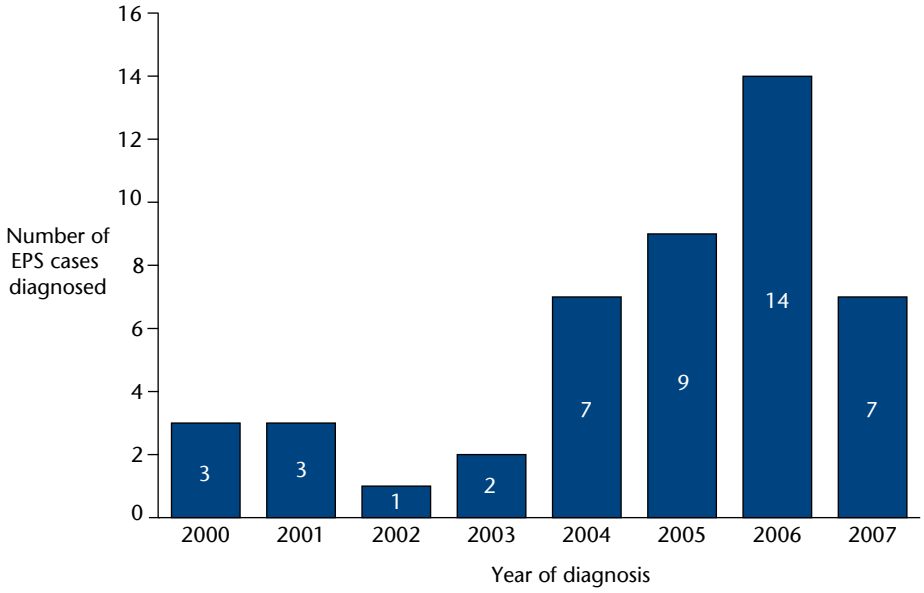
Beyond 4 years of PD there is a marked increase in the proportion of patients developing EPS (1 in 12 patients). The odds ratio of developing EPS with a PD exposure of >2-4 years versus ≤ 2 years is 10.4 (2.2-49.4) and for >4 years versus >3-4 years exposure is 3.2 (1.2-8.6). By 5 years the cumulative risk is 2.6%.

G9.3 Number of EPS cases by renal unit



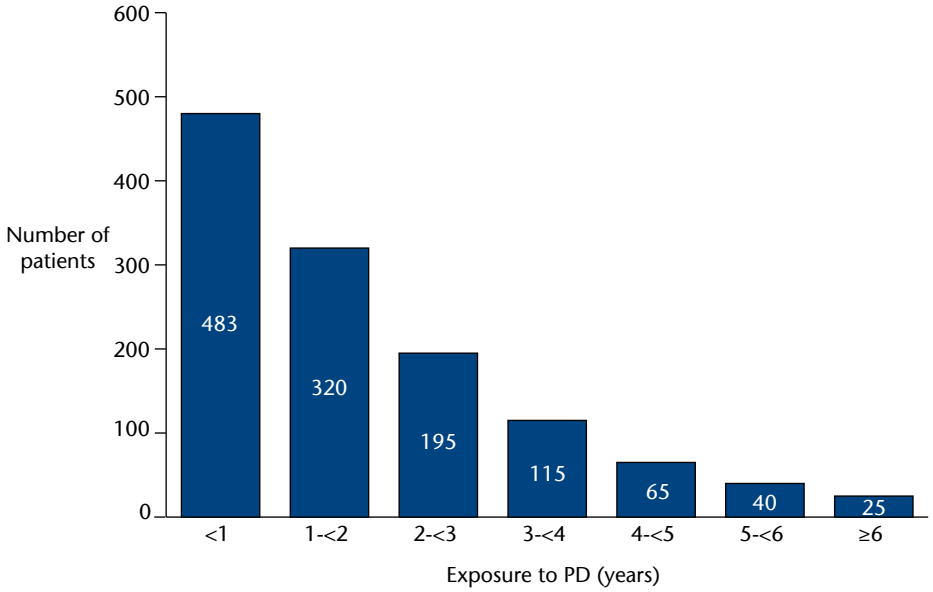
Two units had no confirmed EPS cases diagnosed during the study period. This figure does not take account of the number of prevalent PD patients in each unit.

G9.4 EPS cases by year of diagnosis

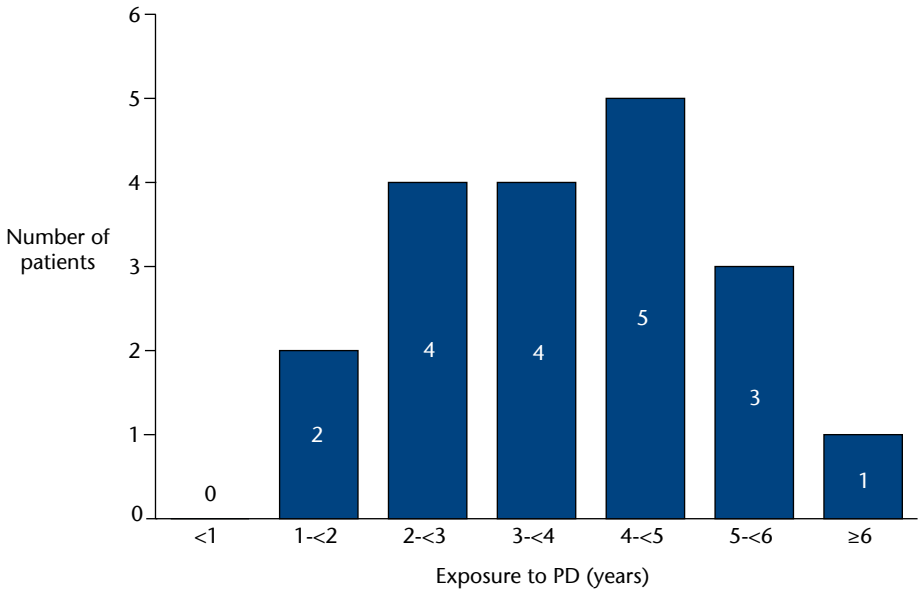


Thirty-seven (80%) of the cases were diagnosed in or after 2004.

G9.5a Duration of PD in patients who did not develop EPS

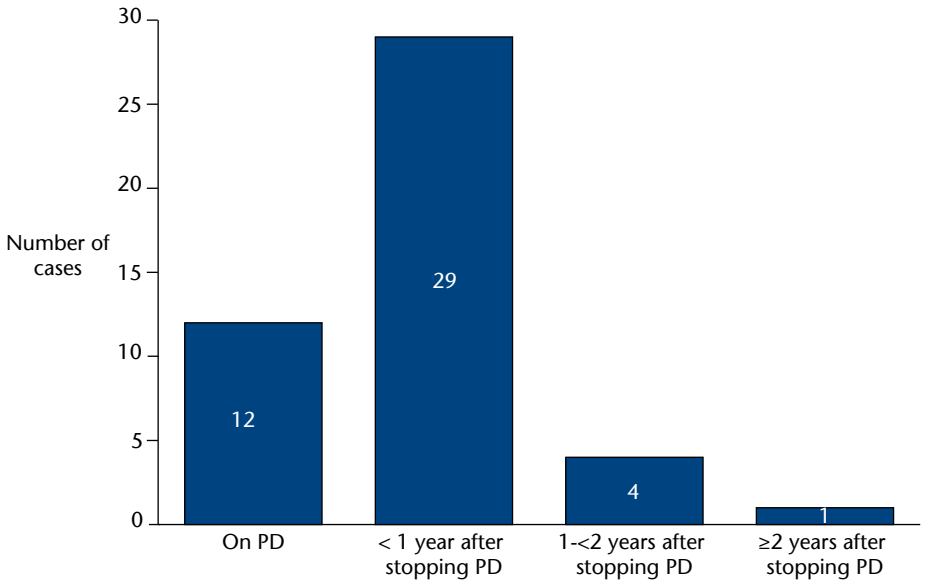


G9.5b Duration of PD in patients who developed EPS



There is a significant association between duration of PD and EPS within Group A ($p< 0.001$). The median duration of PD prior to EPS diagnosis (not necessarily continuous) was 5.1 (range 1.1 – 12.2, IQR 3.4 - 6.1) years. For 1219 patients unaffected by EPS, the median PD duration was 1.3 years (range 1 day - 7.9 years, IQR 0.6 - 2.5 years) whilst for Group B the median PD duration was 3.6 (range 1.1 – 6.1, IQR 2.9-4.9) years.

G9.6 Timing of EPS diagnosis in relation to PD therapy



Twenty-eight (61%) had been on automated peritoneal dialysis. Twenty-two (50%) cases had been transplanted before their EPS diagnosis and in 6 cases the transplant was functioning at diagnosis. Fourteen (30%) were diagnosed within 3 months of peritonitis and in 11 (24%) this episode was severe enough to merit PD catheter removal.

G9.7 Most common presenting clinical features in the EPS cases

Clinical feature	Number of patients
Abdominal pain	30
Vomiting	28
Weight loss	24
Ascites	15
Raised CRP/WCC	14
Bowel obstruction	12
Hypoalbuminaemia	10
Unexplained anaemia	10
Bloody ascites/dialysate	4
Abdominal mass	4
Diarrhoea	4

There is no significant association with age or sex and EPS. Twenty five (54%) were male, 43 (94%) caucasian and the median age at diagnosis was 50 (range 23-82, IQR 42-61) years. Forty two cases (91%) had imaging consistent with EPS 29 (63%) patients had a laparotomy or laparoscopy confirming the diagnosis.

There were no consistent diagnoses in the past medical history to link the cases.

Four patients had no history of peritonitis. For Group A, the median number of peritonitis episodes was 3 (range 0-20, IQR 1 - 4.5) episodes equating to 1 episode every 20 months PD exposure and for Group B the rate is 1 episode every 17 months. The rate in all PD patients in Scotland 2000-2007 was 1 episode every 20 months. The differences in these rates were not statistically significant (relative risk=1.18, 95% confidence interval 0.9-1.57).

In Group A, 16 (35%) had documented prior episodes of Staphylococcus aureus peritonitis (1 MRSA), 5 (11%) fungal peritonitis and 1 (2%) Pseudomonas peritonitis. The 2 patients who developed EPS despite less than 18 months PD had 1 peritonitis episode each, caused by coagulase negative Staphylococci in both cases.

Thirty patients (65%) had used high strength dextrose (3.86%) and 45 (98%) had used Extraneal®. No patients were treated solely with "bio-compatible" dialysate fluids. Various brands of dextrose-based dialysate were used by the EPS cases.

Previous studies implicated beta-blocker drugs in the pathogenesis of EPS. Of our EPS cases, 31 (67%) had been prescribed beta-blockers whilst 15 had not. Other studies have suggested that ACE-inhibitors/angiotensin receptor blocker drugs (ARBs) may preserve the peritoneum and reduce peritoneal fibrosis but this has not been studied in a clinical context. We have details of ACE-inhibitor and angiotensin receptor blocker (ARB) drug prescriptions for some cases: 11/18 (61%) were not prescribed either drug whilst on PD, 4 (22%) were prescribed an ACE or an ARB for the duration of PD treatment and 3 were prescribed one or other for <50% of time on PD. Gadolinium contrast used in MRI scanning can cause another fibrosing condition; nephrogenic systemic fibrosis. No studies have looked for any association with EPS. We had access to complete radiology records for 34 patients, and only 6 of these (18%) had had an MR scan prior to diagnosis of EPS.

G9.8 Drug therapy prescribed to treat EPS or as part of transplant immunosuppression	
Treatment/Transplant status	**Number of cases**
Tamoxifen only	6
Sirolimus	3*
Prednisolone + Tamoxifen	4
Tamoxifen + Azathioprine	1
Prednisolone + Azathioprine	1
Functioning transplant (Tamoxifen added)	6 (2)
Transplanted <4 months post-diagnosis	4
Total treated with Tamoxifen	13
Total Treated with immunosuppression	24

* In 1 case Sirolimus was used as part of post-transplant immunosuppression.

Table G9.8 details the drugs prescribed to treat the EPS cases. It was beyond the scope of this study to assess response to treatment. Only 3 patients had elective surgical intervention. By the study end on 31 December 2007, 26 of the patients with EPS (57%) had died. The mortality rate was 42% at one year after diagnosis. The median survival from diagnosis was 180 (range 1 – 1075, IQR 61 – 408) days.

Conclusions

The incidence of EPS is higher than described previously, particularly for patients with less than 5 years of PD exposure. Using our data, the risk of EPS for patients treated with PD in Scotland is near zero after 1 year of PD but the minimum risk after 4 years of PD is 1 in 12. However, the cumulative risk is modest at 2.6% by 5 years, reflecting the fact that relatively few patients continue PD beyond 4 years. The incidence reported in this study may be used to inform patients of the minimum risk of developing EPS after starting PD.

This work has been published[12].

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