

# A simple model to predict encapsulating peritoneal sclerosis in patients undergoing peritoneal dialysis: a 20 years prospective controlled longitudinal cohort study of peritoneal membrane function

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## OBJECTIVES

Encapsulating peritoneal sclerosis (EPS) is an uncommon but severe complication of peritoneal dialysis (PD) and mortality rate without therapy is about 50%. EPS has a good prognosis, if treated early. No screening tool is already reliable.

The reduction of free-water transport (FWT) can reflect both structural and functional damage of the peritoneal membrane. The reduction in dialysate sodium concentration, at 60 minutes ( $\Delta_{Na60}$ ), during a peritoneal equilibration test with 3.86% glucose concentration (3.86%-PET), is the simplest indirect method to assess FWT. The aim of this study was to evaluate whether the  $\Delta_{Na60}$ , alone or in association with other parameters, is able to early detect patients who develop EPS.

## RESULTS

During the follow-up, we studied 161 patients (male/female: 80/81, CAPD/APD: 107/54), median age 59.0 (50.5- 69.5) years at start of PD, median duration of PD 37.8 (24.7-58.3) months and 64.1 (34.5-108.3) months of follow-up. A total of 498 test (3.86%-PET) were performed in our PD patients during the long period of follow-up. 13 patients (8%) developed EPS (male/female: 3/10, CAPD/APD: 7/6), median age 49 (43-61) years at start of PD, median duration of PD 72.7 (56.6-109.4) months and 105.0 (76.4-143.2) months of follow-up. At multivariate analysis,  $\Delta_{Na60}$  was the only powerful and independent risk factor associated with EPS (Table I) about 1 year before the onset of EPS. Tables II, III and IV shows sensitivity, specificity, positive predictive value and negative predictive value of single parameters obtained with the PET, about 1, 2 and 3 years before the onset of EPS. At the multifactorial analysis, the best ROC curves were obtained considering age at PD start, PD duration,  $D/P_{Creat}$  and  $\Delta_{Na60}$ , about 1 (a), 2 (b) and 3 (c) years before the onset of EPS, while the prediction was not improved by adding to the model sex, peritonitis rate, UF and  $D/D_0$  (Tables V and Figure 1). Figure 2 show how we can use the most significant parameters of ROC curve for predicting the onset or less of EPS about 1 year before the onset of EPS.

Table I. Multivariate analysis performed using a logistic regression random-effects model and including potential risk factors for EPS about 1 year before the onset of EPS (or before the end of the PD or censoring time in patients without EPS)

Characteristic	Coefficient (95% Confidence Interval)	P value
Sex	-1.88 (-1.96 to -1.81)	0.11
Age at PD start	0.16 (0.15 to 0.17)	0.07
PD duration	-0.17 (-0.18 to -0.17)	0.05
Peritonitis rate	1.26 (1.27 to 1.31)	0.09
$D/P_{Creat}$	-27.96 (-29.48 to -26.44)	0.25
$D/D_0$	3.6 (2.30 to 4.89)	0.86
UF	$0.10 \times 10^{-2}$ ( $0.09 \times 10^{-2}$ to $0.12 \times 10^{-2}$ )	0.66
$\Delta_{Na60}$	1.26 (1.22 to 1.30)	0.04

Table II. Sensitivity, specificity positive predictive value and negative predictive value of the individual parameters obtained with the PET, age at PD start and time on PD, about 1 year before the onset of EPS or the end of the PD or censoring time (161 patients)

	Sensitivity	Specificity	Youden	PPV	NPV
$\Delta_{Na60} \leq 4.8$ mmol/L	100% (75-100%)	73% (65-80%)	0.73	0.25	1.00
Age at start of PD $\leq 51$ years	62% (32-86%)	76% (68-82%)	0.37	0.18	0.96
Time on PD $> 29$ months	100% (75-100%)	59% (50-67%)	0.59	0.18	1.00
$D/P_{Creat} > 0.72$	100% (75-100%)	57% (49-66%)	0.57	0.17	1.00
$D/D_0 \leq 0.17$	77% (46-95%)	78% (71-85%)	0.55	0.24	0.98
$UF \leq 612$ mL	92% (64-100%)	66% (58-74%)	0.59	0.19	0.99

Table III. Sensitivity, specificity positive predictive value and negative predictive value of the individual parameters obtained with the PET, age at start of PD and time on PD, about 2 years before the onset of EPS or the end of the PD or censoring time (120 patients)

	Sensitivity	Specificity	Youden	PPV	NPV
$\Delta_{Na60} \leq 6.2$ mmol/L	92% (64-100%)	66% (57-75%)	0.59	0.25	0.97
Age at start of PD $\leq 51$ years	62% (32-86%)	76% (67-84%)	0.37	0.24	0.94
Time on PD $> 40$ months	69% (39-91%)	82% (74-89%)	0.51	0.32	0.96
$D/P_{Creat} > 0.74$	85% (55-98%)	68% (59-77%)	0.53	0.24	0.97
$D/D_0 \leq 0.19$	77% (46-95%)	68% (58-77%)	0.23	0.24	0.96
$UF \leq 536$ mL	69% (39-91%)	82% (74-89%)	0.51	0.32	0.96

## METHODS

We studied all incident patients starting PD at our Department from January 1994 to December 2014. In all these patients, a 3.86%-PET was performed during the first 12 months from the start of PD and then once a year. During 3.86%-PET we evaluated peritoneal ultrafiltration (UF), the absorption of glucose ( $D/D_0$ ), transport of small solutes ( $D/P_{Creat}$ ) and  $\Delta_{Na60}$ . To avoid reduced exposure to the risk associated with PD, patients with less than 12 months duration of PD and patients who had a follow-up of less than 12 months after completion of the last 3.86%-PET were excluded. We selected only patients with definite EPS (surgically or radiologically confirmed peritoneal membrane thickening and cocooning, in conjunction with weight loss and features of bowel obstruction).

Table IV. Sensitivity, specificity, positive predictive value and negative predictive value of the single parameters obtained with the PET, age at start of PD and time on PD, about 3 years before the end of the PD or the onset of EPS or censoring time (85 patients)

	Sensitivity	Specificity	Youden	PPV	NPV
$\Delta_{Na60} \leq 6.9$ mmol/L	85% (55-98%)	82% (71-90%)	0.67	0.46	0.97
Age at start of PD $\leq 51$ years	62% (32-86%)	75% (63-85%)	0.37	0.31	0.92
Time on PD $> 28$ months	69% (39-91%)	72% (60-82%)	0.51	0.31	0.93
$D/P_{Creat} > 0.71$	100% (75-100%)	69% (58-80%)	0.69	0.37	1.00
$D/D_0 \leq 0.21$	85% (55-98%)	53% (41-65%)	0.37	0.24	0.95
$UF \leq 802$ mL	92% (64-100%)	49% (37-61%)	0.41	0.25	0.97

Table V. Sensitivity, specificity, positive predictive value (95% confidence interval) and negative predictive value (95% confidence interval) of age at the start of PD, duration of PD,  $D/P_{Creat}$  and  $\Delta_{Na60}$ , considered together, about 1, 2 and 3 years before the onset of EPS or the end of the PD or censoring time

Time before the onset of EPS or the end of the PD or censoring time (years)	Sensitivity	Specificity	Youden	PPV	NPV
1	62%	99%	0.90	0.88 (0.51-1.00)	0.97 (0.93-0.99)
2	46%	97%	0.90	0.65 (0.29-0.92)	0.94 (0.87-0.97)
3	54%	94%	0.75	0.62 (0.30-0.88)	0.92 (0.83-0.97)

Figure 1

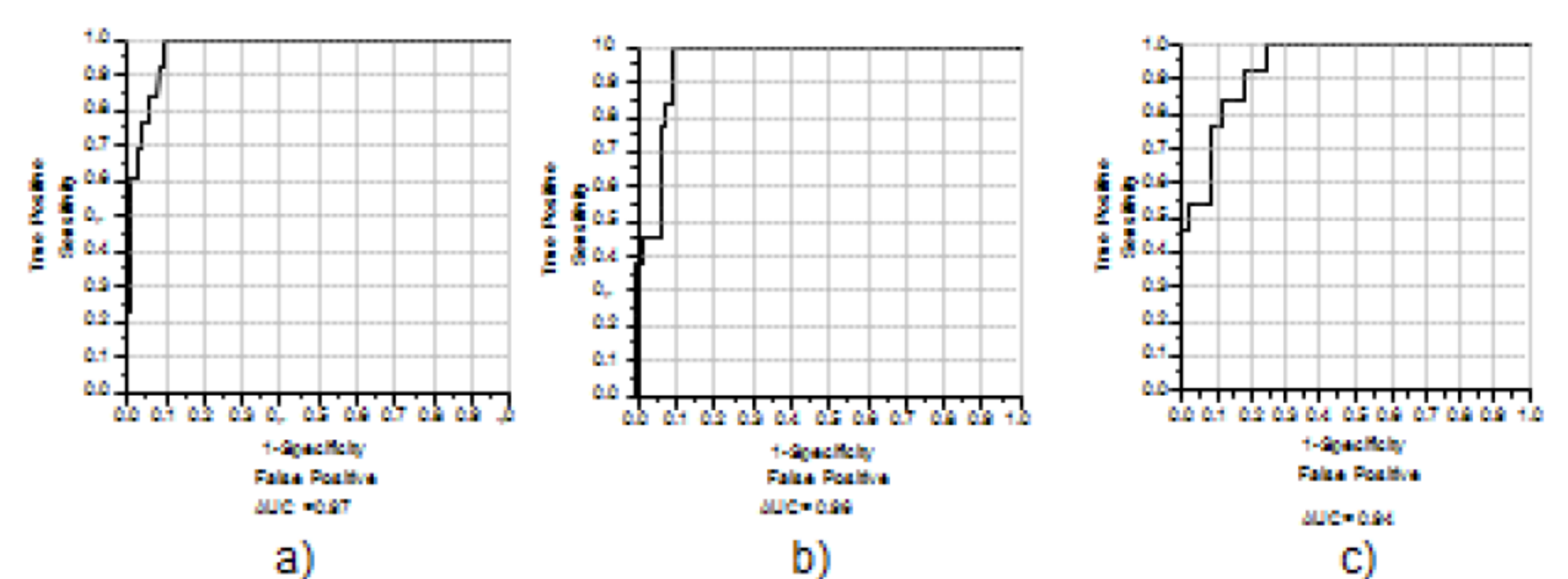
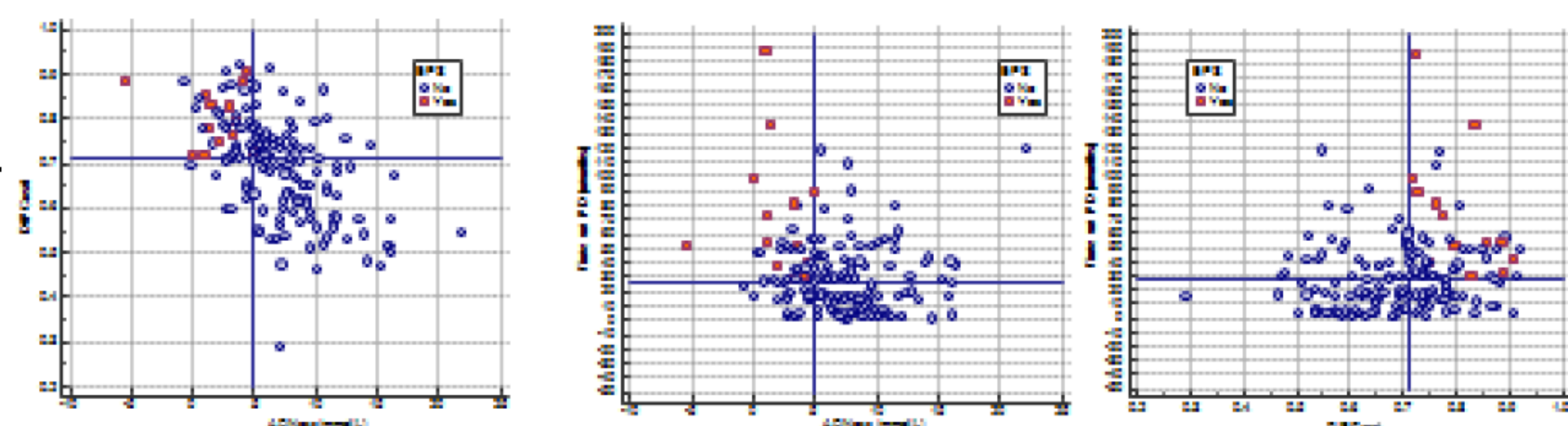


Figure 2



## CONCLUSIONS

It is possible to predict onset or less of EPS, about 1 year, 2 years and 3 years before, using simple parameters such as age at start of PD, duration of PD,  $D/P_{Creat}$  and  $\Delta_{Na60}$  obtained with the 3.86%-PET, avoiding unnecessary drop-out of patients in PD.