self-care dialysis
symposium

A high intraperitoneal residual volume hampers adequate volumetric assessment of osmotic conductance to glucose

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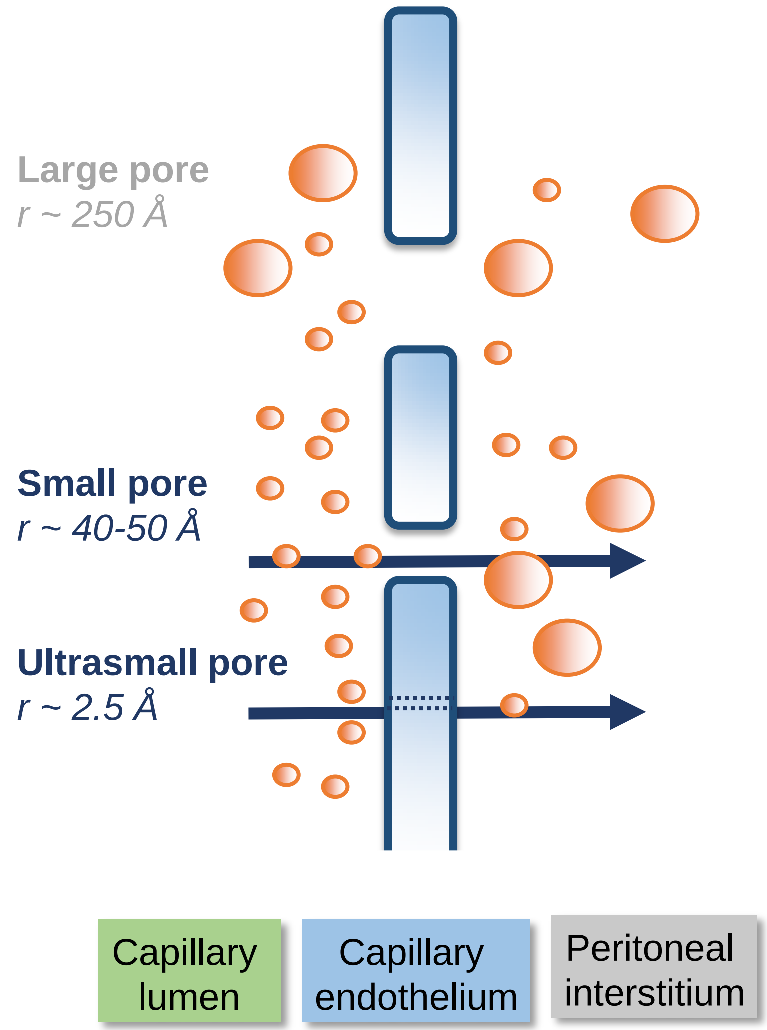
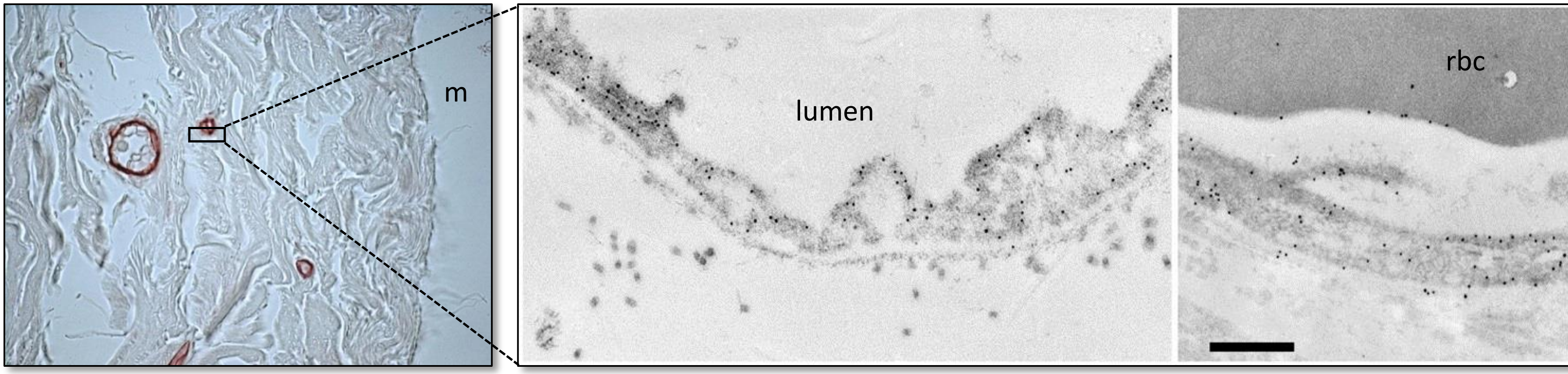
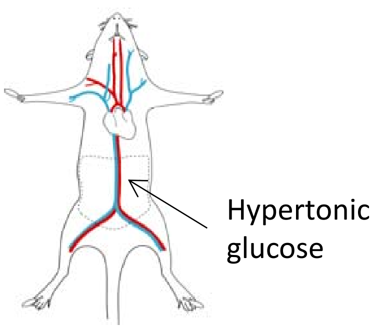
Osmotic water transport across peritoneal membrane

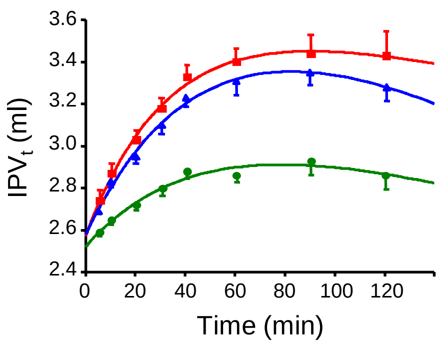
- Water removal (or UF): major determinant of outcome among PD patients
- Generated by osmotic agents in the dialysis solution (glucose *vs* icodextrine)
- Crystalloid osmosis - pathways: 50/50%
  - 'Small pores'/interendothelial junctions (solute-coupled water transport)
  - AQP1 water channels (free-water transport, sodium sieving

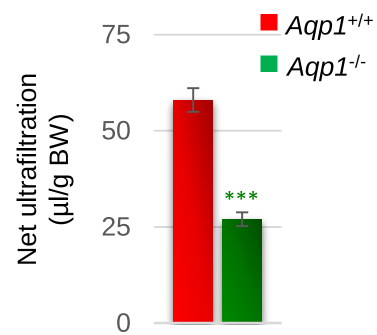


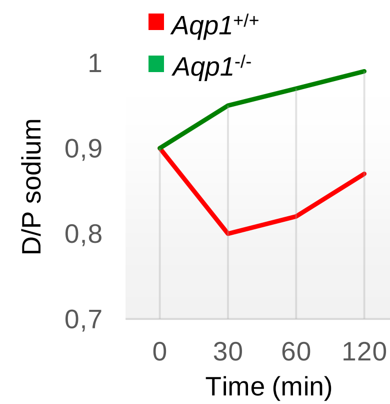
Aquaporin-1 and water transport in PD







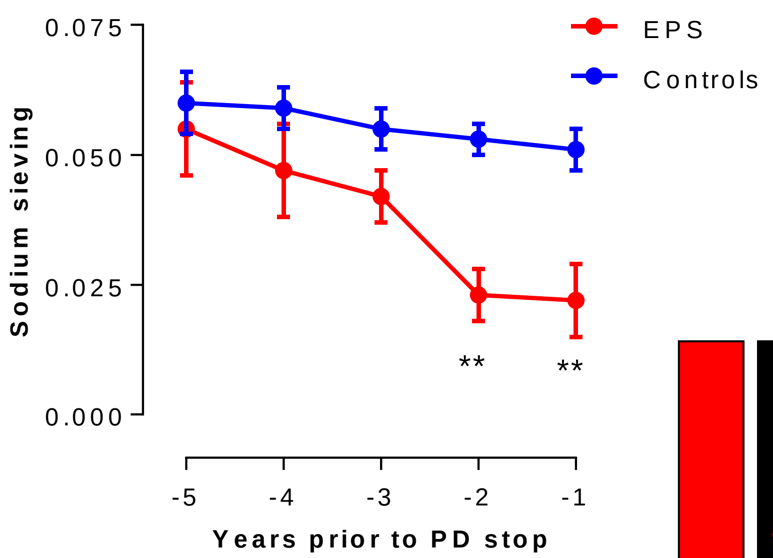




Endothelial AQP1 → ultrasmall pore
50% of water removal and sodium sieving in PD

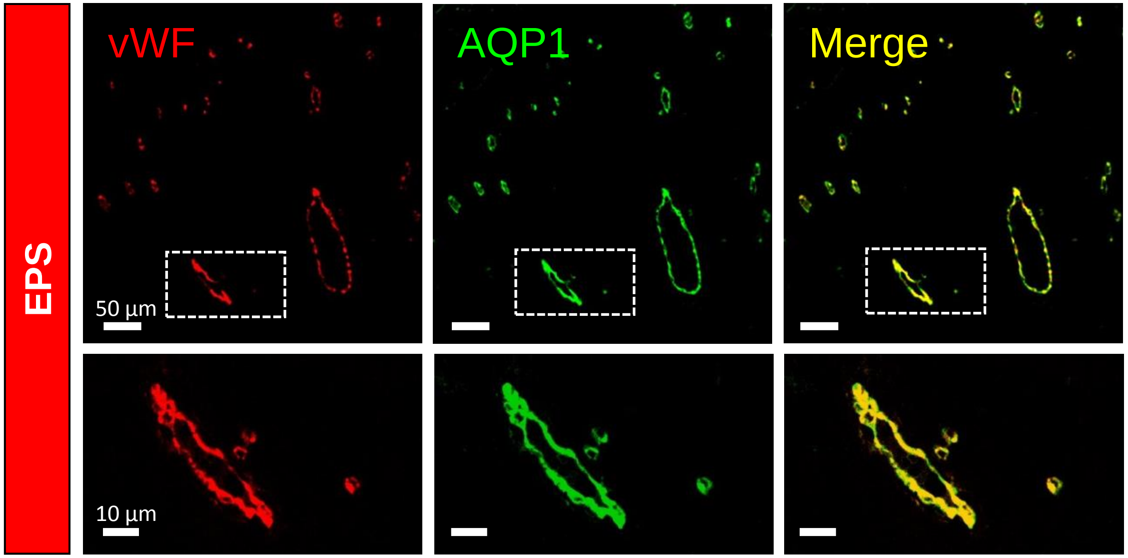
Devuyst et al, *Am J Physiol* 1998 ; Ni et al, *Kidney Int* 2005

EPS and loss of peritoneal osmotic conductance



Patients with EPS

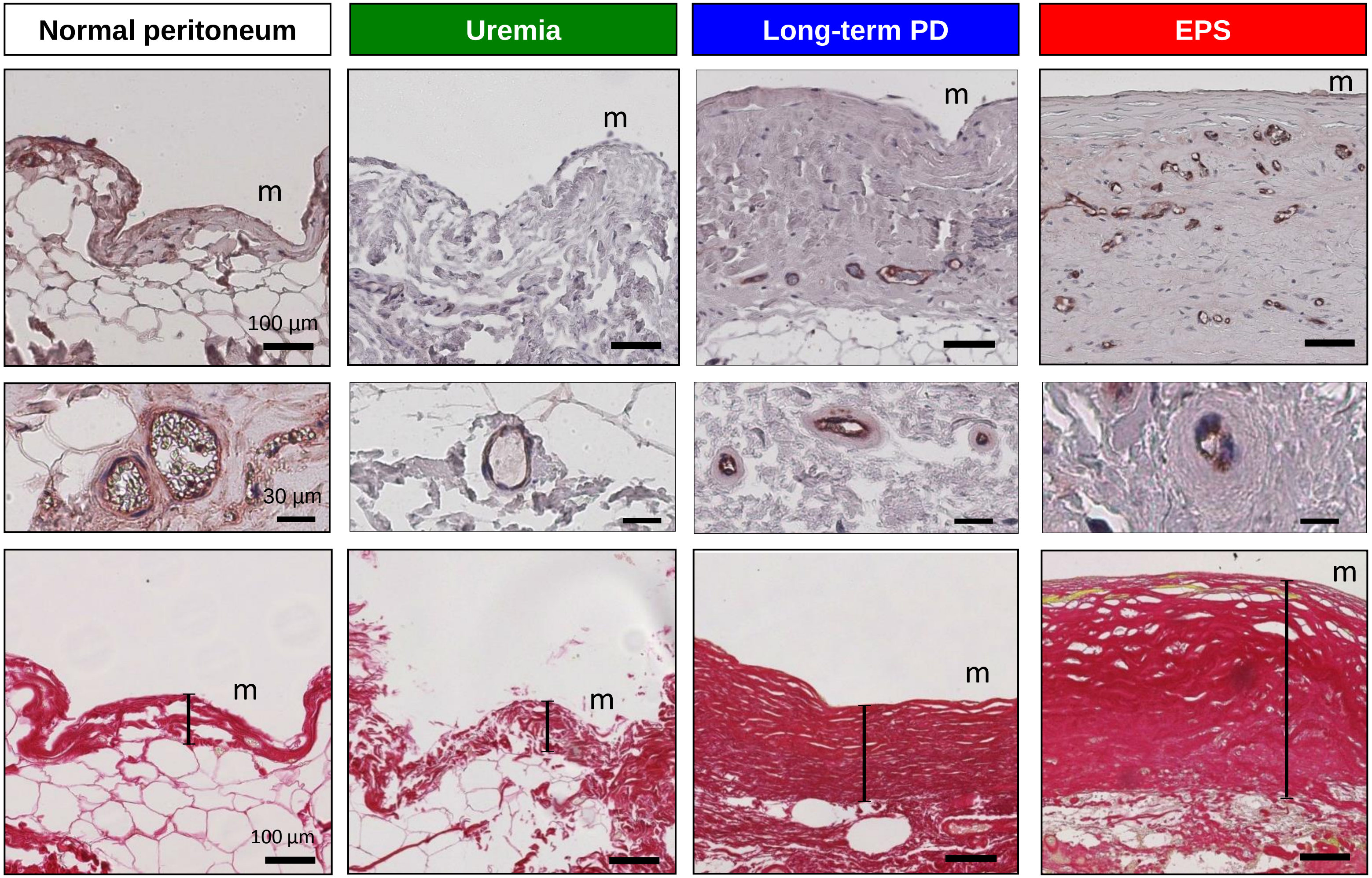
- *Loss of UF (uncoupling with PSTR rise)*
- *Altered sodium sieving*
- *Preserved expression of AQP1*



→ Role for peritoneal fibrosis?

Morelle…Devuyst, Goffin, *J Am Soc Nephrol* 2015

Severe structural alterations in the EPS peritoneum



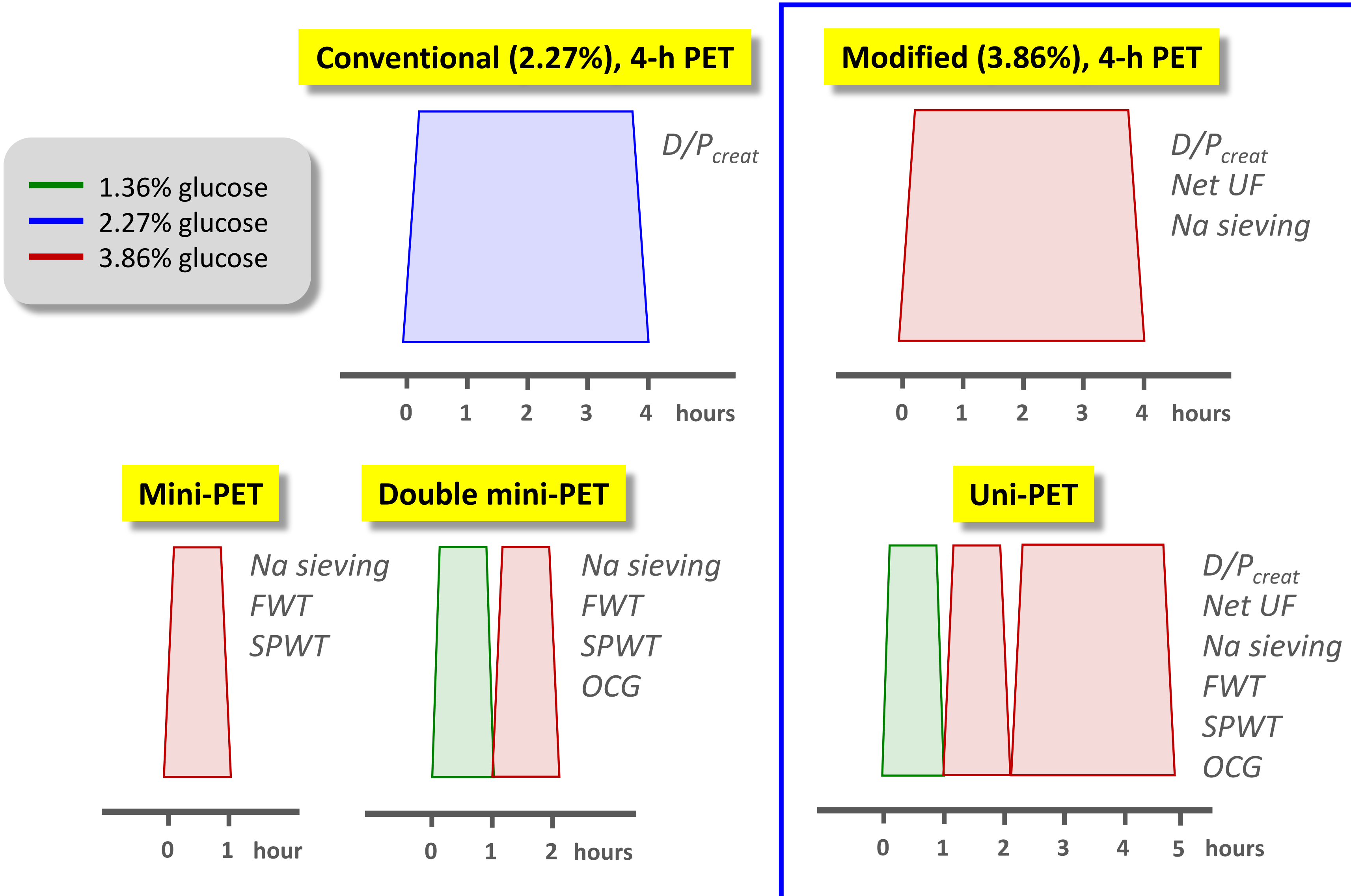
Morelle…Devuyst*, Goffin*, *J Am Soc Nephrol* 2015

Length of Time on Peritoneal Dialysis and Encapsulating Peritoneal Sclerosis: Position Paper for ISPD – Update 2017

'Progressive loss of osmotic conductance to glucose (uncoupling between water and solute transport, altered sodium sieving, decreased free-water transport) may reflect the development of peritoneal interstitial fibrosis and may help identifying patients at risk of EPS'

Edwina A Brown, Joanne Bargman, Wim van Biesen, Ming-Yang Chang, Frederic O Finkelstein, Helen Hurst, David W Johnson, Hideki Kawanishi, Mark Lambie, Thyago Proença de Moraes, Johann Morelle, Graham Woodrow – Perit Dial Int 2017

How to monitor osmotic water transport?

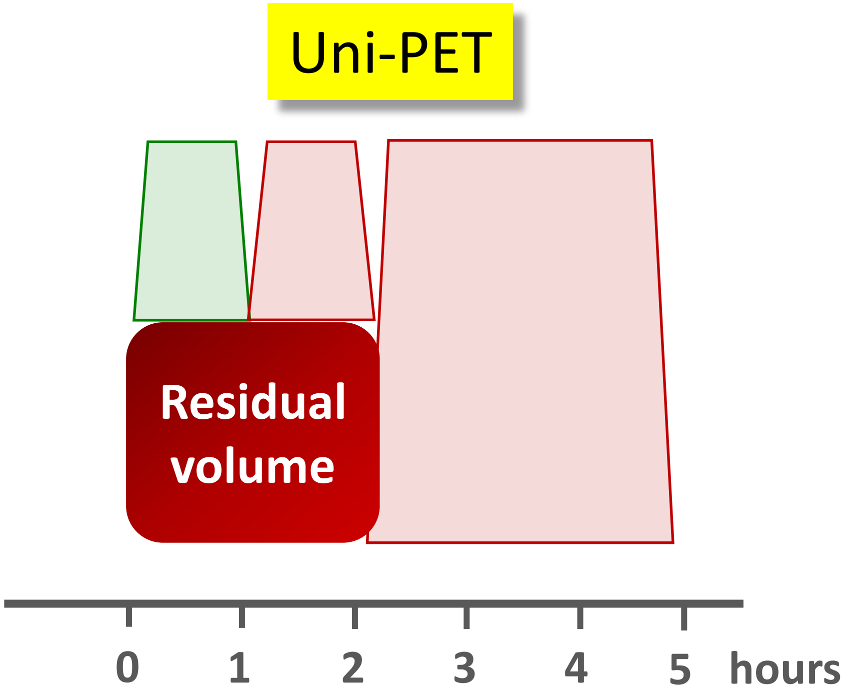


Potential drawback of OCG assessed using the double mini or uni-PET

1. It relies on drained volumes

$$OCG = \frac{(V_{3.86} - V_{1.36})}{19.3 \times (G_{3.86} - G_{1.36}) \times t} \times 1.7$$

2. A large residual volume may potentially interfere with its correct assessment



Influence of the intraperitoneal residual volume on OCG assessment using double-mini PET?

Patients and methods

- Retrospective monocentric study, Cliniques universitaires Saint-Luc, Brussels

- All consecutive ESRD patients:
  - Starting PD between february 2013 and March 2017,
  - For which a Uni-PET was performed within the first 3 months on PD, then yearly,
  - n= 35 patients, 53 tests

- Residual volume assessed using albumin *(dilution method)*

Patients characteristics

Characteristic	Value
No. of patients	35
Age at PD start - years	45 ± 15
APD - n (%)	23 (66)
Ethnicity - n (%)	
Caucasian	30 (86)
African	2 (6)
Asian	3 (8)
Female gender – n (%)	14 (40)
BMI – kg/m²	24 ± 4
Systolic BP – mmHg	140 ± 20
Diastolic BP – mmHg	87 ± 13
Residual urine volume - ml/day	1567 ± 660
Mean of renal urea and CrCl – ml/min	7 ± 4

Characteristic	Value
Charlson comorbidity index	5 ± 3
Davies comorbidity index	1 ± 1
Hypertension - n (%)	31 (89)
Diabetes - n (%)	10 (29)
History of CHF - n (%)	1 (3)
History of CHD - n (%)	4 (11)
Kidney transplant waiting list - n (%)	27 (77)
Albumin - g/L	37 ± 4
Underlying nephropathy - n (%)	
Glomerulonephritis	13 (37)
Chronic interstitial nephritis	8 (23)
Polycystic kidney disease	2 (6)
Reno-vascular disease	1 (3)
Diabetic nephropathy	7 (20)
Miscellaneous nephropathy	4 (11)
Chronic treatment	
ACEi - n (%)	16 (46)
ARB - n (%)	10 (29)
Beta-Blockers - n (%)	10 (29)
Corticosteroids - n (%)	8 (23)

Continuous variables are mean ± SD and categorical variables, number (n) and percentage (%). PD, peritoneal dialysis; APD, automated PD; BMI, body mass index; BP, blood pressure; RRF, residual renal function; CrCl, creatinine clearance; CHF, congestive heart failure; CHD, coronary heart disease; ACEi, angiotensin-converting-enzyme inhibitor; ARB, angiotensin II receptor blockers.

Parameters of peritoneal transport at baseline, 12 and 24 months

	Baseline n= 34	12 months n = 15	24 months n = 4
Net UF 3.86% glucose – ml/4h	524 ± 305	504 ± 222	614 ± 86
D/P_{creat} at 4h	0.70 ± 0.12	0.68 ± 0.09	0.67 ± 0.07
Dip Na 60 min - mmol/L	9 ± 4	8 ± 2	8 ± 4
ΔD/P Na 60 min	0.06 ± 0.03	0.06 ± 0.02	0.06 ± 0.03
FWT - ml	174 ± 100	156 ± 41	164 ± 70
SPWT - ml	149 ± 110	134 ± 153	200 ± 89
OCG - µl/min/mmHg	3.9 ± 1.4	3.4 ± 2.0	4.5 ± 0.7
Residual volume - ml	492± 201	553 ± 160	505 ± 113

Data are mean ± SD. UF, ultrafiltration; D/P_{creat}, dialysate-over-plasma creatinine ratio; FWT, free-water transport; small pore-water transport; OCG, osmotic conductance to glucose

1. Correlation between the different parameters of osmotic water transport?

	Net UF 4h	ΔD/P Na 60 min (stock)	ΔD/P Na 60 min (t0)	Dip Na 60 min (stock)	Dip Na 60 min (t0)	FWT	OCG
Net UF 4h	1.00						
ΔD/P Na 60 min (stock)	**0.41****	1.00					
ΔD/P Na 60 min (t0)	**0.38****	**0.82*****	1.00				
Dip Na 60 min (stock)	**0.42****	**0.99*****	**0.83*****	1.00			
Dip Na 60 min (t0)	**0.40****	**0.83*****	**1.00*****	**0.83*****	1.00		
FWT	**0.52****	**0.94*****	**0.81*****	**0.95*****	**0.82*****	1.00	
OCG	-0.00	-0.09	-0.09	-0.08	-0.09	0.08	1.00

*P<0.05, **P<0.01, ***P<0.001. UF, ultrafiltration; D/P, dialysate-over-plasma ratio; FWT, free-water transport; OCG, osmotic conductance to glucose.

OCG assessed using the double mini-PET does not correlate with any of the other parameters of osmotic water transport

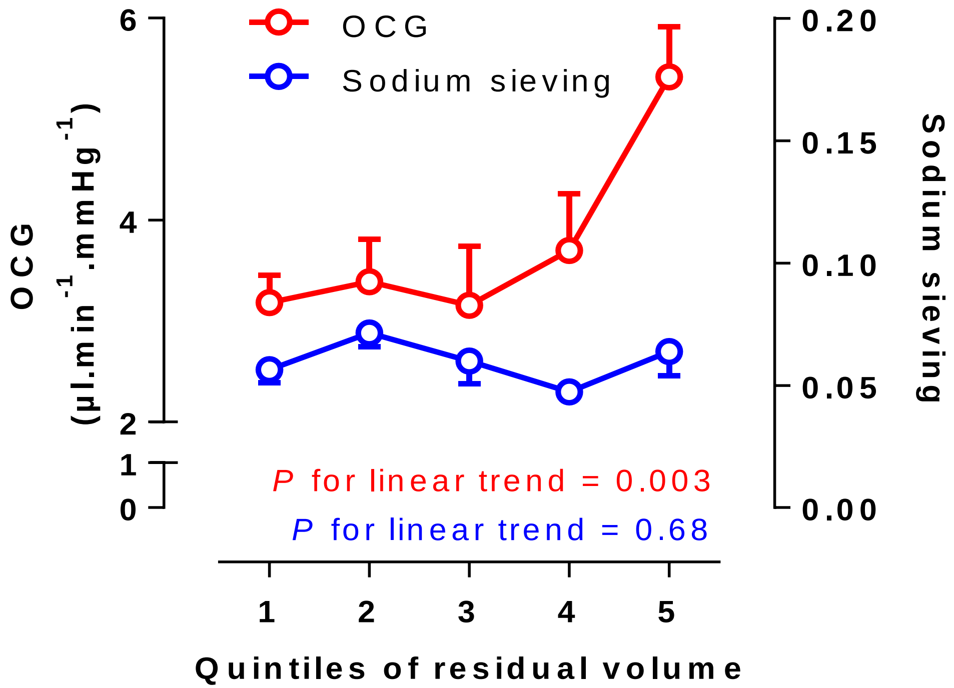
2. Determinants of the parameters of osmotic water transport (multivariate regression analysis)?

	Model 1			Model 2		
	Coeff.	95% CI	*P*	Coeff.	95% CI	*P*
Sodium sieving						
D/P_{creat} at 4h	**-0.09**	**-0.16 – -0.03**	**0.006**	**-0.09**	**-0.16 – -0.02**	**0.009**
RRF	**-0.003**	**-0.005 – -0.001**	**0.002**	**-0.003**	**-0.005 – -0.001**	**0.002**
Residual volume	-	-	-	-7.2×10^{-6}	-4.3×10^{-5} – 2.9×10^{-5}	0.691
Free-water transport						
D/P_{creat} at 4h	**-299.2**	**-485.0 – -113.4**	**0.002**	**-303.6**	**-495.0 – -112.7**	**0.002**
RRF	**-7.4**	**-12.6 – -2.2**	**0.006**	**-7.4**	**-12.7 – -2.2**	**0.006**
Residual volume	-	-	-	1.3×10^{-2}	-0.1 –0.1	0.799
Osmotic conductance						
D/P_{creat} at 4h	-0.1	-4.5 – 4.3	0.963	-1.8	-5.9 – 2.4	0.395
RRF	0.0	-0.1 – 0.1	0.767	-0.02	-0.13 – 0.10	0.753
Residual volume	-	-	-	**4.1×10^{-3}**	**1.6×10^{-3} – 6.6×10^{-3}**	**0.002**

Coeff., coefficient; 95% CI, 95% confidence interval; D/P_{creat}, dialysate-over-plasma creatinine ratio; RRF, residual function, based on the mean of renal urea and creatinine clearances.

RV is the only and independent determinant of OCG

3. Relationship between the residual volume and OCG, and the residual volume and sodium sieving



OCG progressively increased with increasing intraperitoneal residual volume while sodium sieving remained unchanged

Conclusions

- Importance of regular monitoring of peritoneal water transport by using double mini-PET to detect progressive fibrosis (functional « exhaustion » of the peritoneal membrane)
- However OCG assessed using the double mini-PET does not correlate with any of the other osmotic water transport parameters
- The only powerful determinant of OCG is the RV!
- Potential artificial overestimation of the OCG in patients with high RV, limiting its sensitivity to detect fibrogenic changes in the peritoneal membrane and to identify patients at risk for EPS.
- Na Sieving *(biochemical surrogate for OCG)* may be a more reliable parameter than OCG

Discussion

- High RV affects volumetric assessment of the OCG through initial underestimation of the net UF during the 1.36% glucose-based dwell

- Limitations of our study:

  - Monocentric design, samples size
  - No determined « cut-off » of RV for correct interpretation of OCG
  - No determination of RV with exogenous indicator

- Perspectives: prospective multicentre studies with Paris-Bichat, Vichy, Caen, Pitié Salpêtrière, Besancon to validate these conclusions and determine criteria for a correct interpretation of OCG

Acknowledgments

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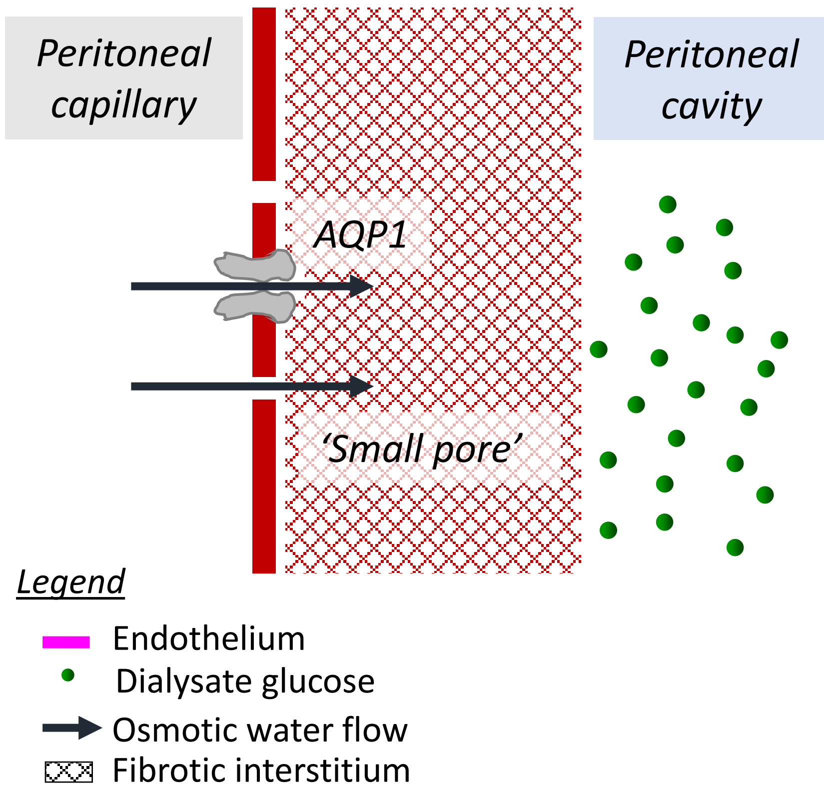
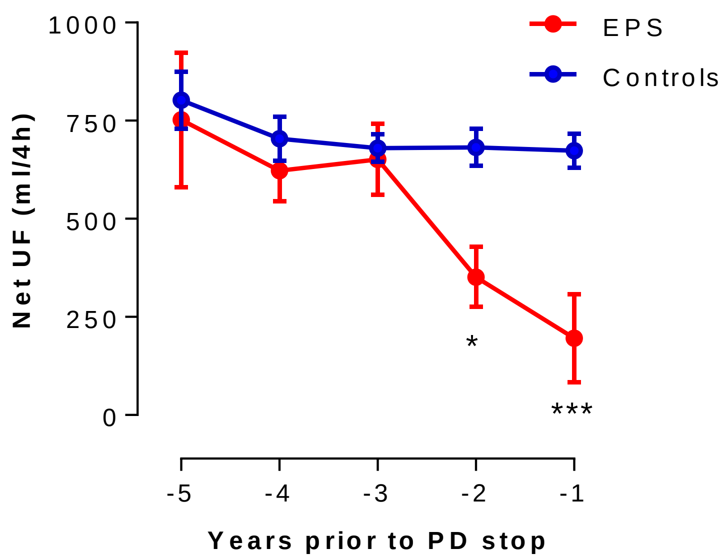
- Nursing Home dialysis “DEH”
- Caroline Berghe and Veronique Van Hole (Study Nurses)

Thank you for your attention !

EPS and loss of peritoneal osmotic conductance

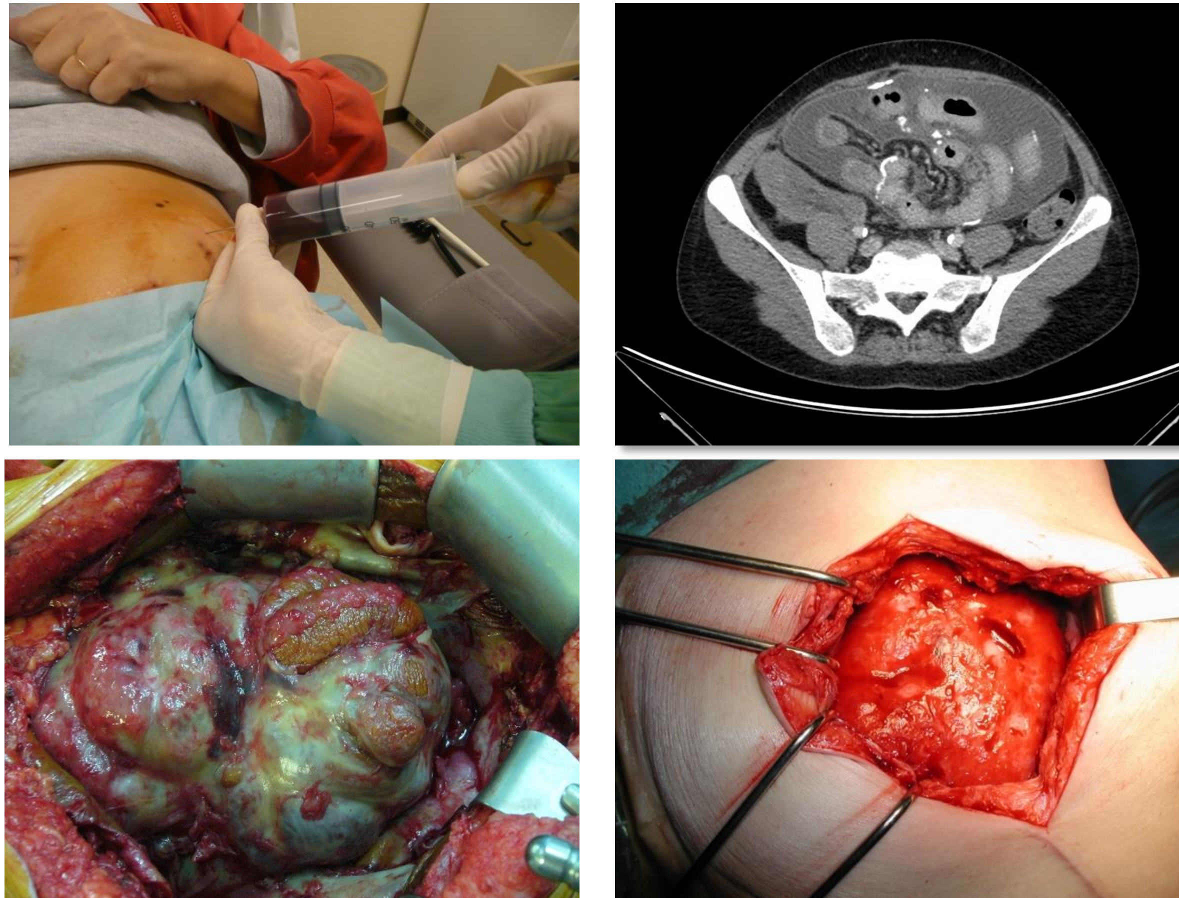
234 incident PD patients, 1994-2013, Saint-Luc Academic Hospital, Brussels
7 patients with EPS *versus* 28 (4:1) matched controls – yearly 3.86% glucose-based PET





Morelle…Devuyst, Goffin, *J Am Soc Nephrol* 2015

Encapsulating peritoneal sclerosis (EPS)

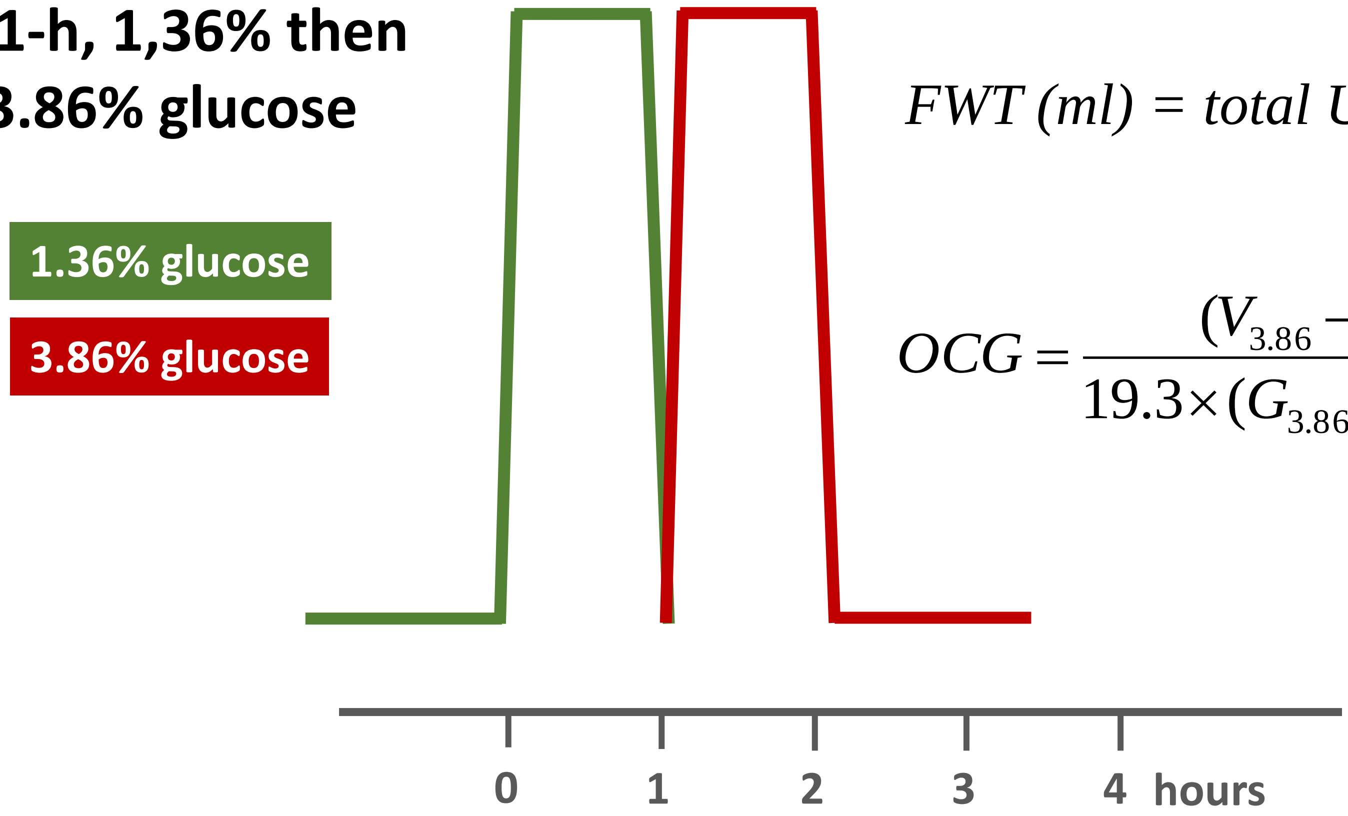


Devastating syndrome of excessive fibrotic peritoneal thickening that can eventually encapsulate the bowel, leading to partial or total bowel obstruction

Courtesy Prof. C. Verger, T. Augustine, J.Morelle and E. Goffin

A simple method to directly calculate OCG and FWT: the double mini-PET

2x1-h, 1,36% then 3.86% glucose

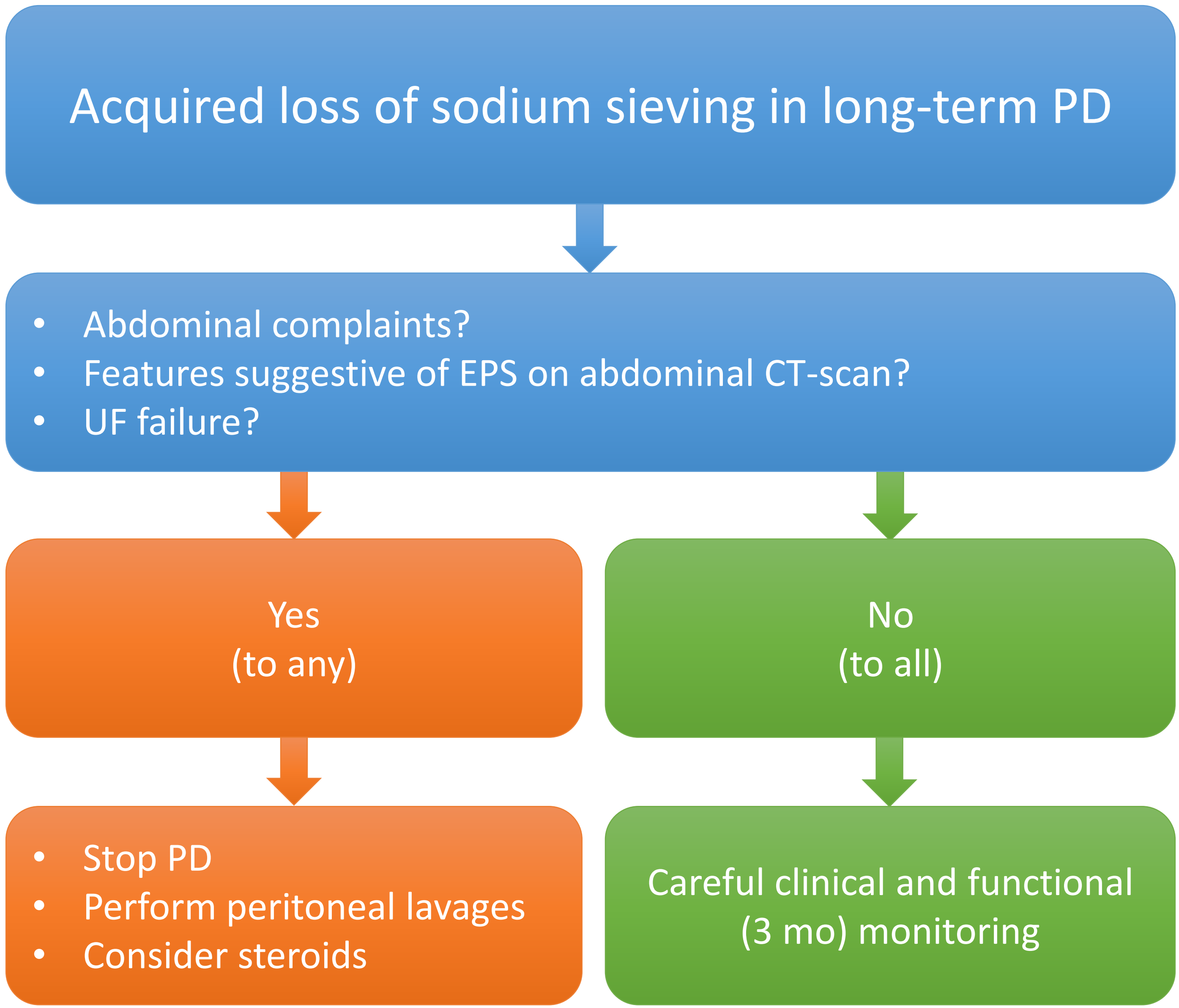


$$FWT\ (ml) = total\ UF - UFSP$$

$$OCG = \frac{(V_{3.86} - V_{1.36})}{19.3 \times (G_{3.86} - G_{1.36}) \times t} \times 1.7$$

Osmotic conductance to glucose (OCG, ml x min^{-1} x mmHg^{-1})
= « the amount of UF that can be obtained by increasing the concentration of glucose in the dialysate »

La Milia et al, Kidney Int 2007


Acquired loss of sodium sieving in long-term PD
Abdominal complaints?
Features suggestive of EPS on abdominal CT-scan?
UF failure?
Yes
(to any)
No
(to all)
Stop PD
Perform peritoneal lavages
Consider steroids
Careful clinical and functional
(3 mo) monitoring