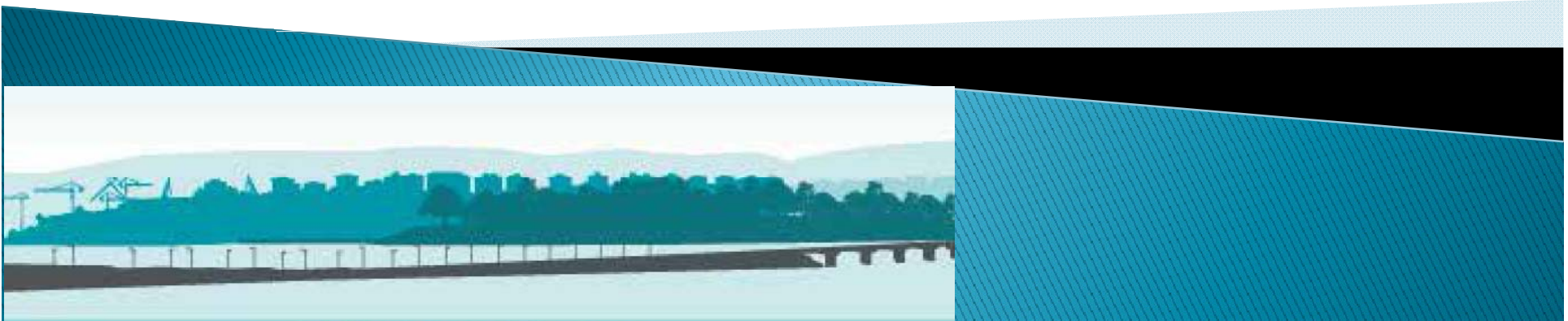


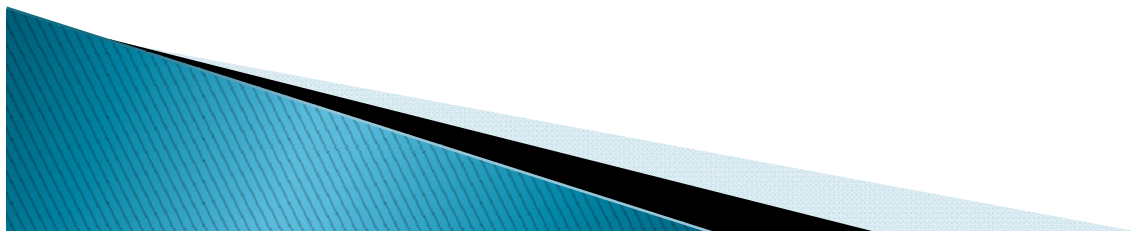
Manejo del paciente con problemas de ultrafiltración

Ana Rodríguez-Carmona de la Torre
CHU A Coruña

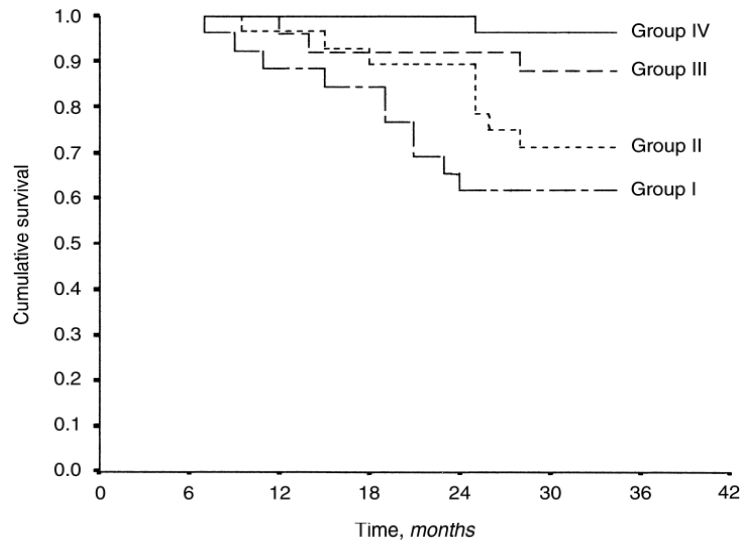


SUMARIO

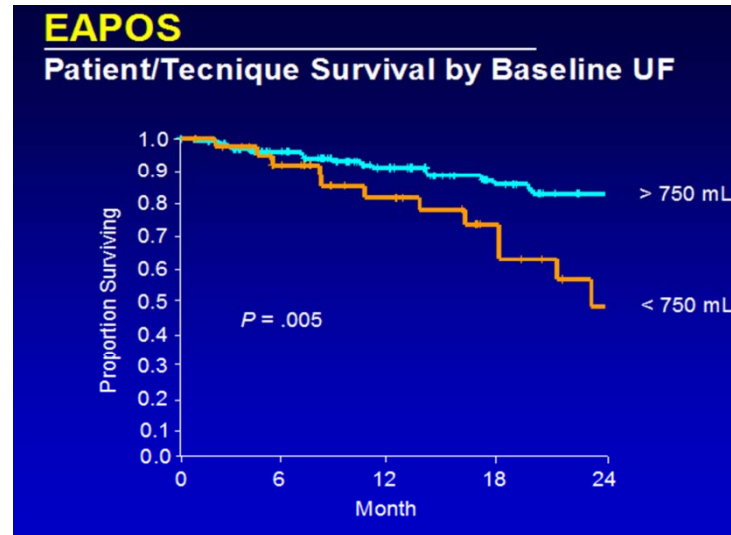
- ▶ Importancia de la ultrafiltración
- ▶ Mecanismos de la ultrafiltración en DP
- ▶ Definición de fallo de UF
- ▶ Componentes del transporte de agua y como estudiarlos
- ▶ Tipos de fallo de UF
- ▶ Prevención
- ▶ Manejo del paciente con fallo de UF



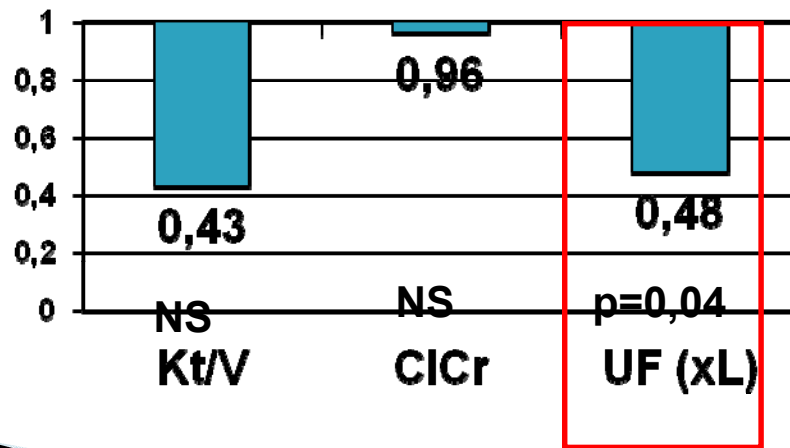
Mortalidad según UF



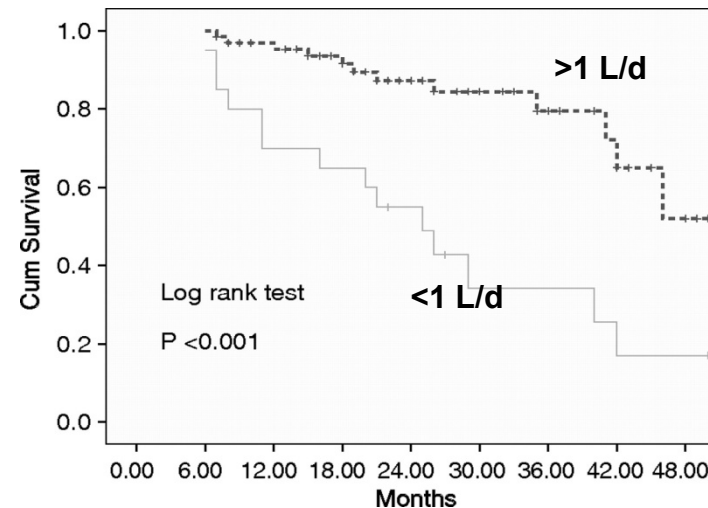
Ates. *Kidney Int* 2001; 60: 767



Brown. *J Am Soc Nephrol* 2003; 14: 2948



Jansen. *Kidney Int* 2005; 68: 1199



Lin, X. et al. *Nephrol. Dial. Transplant.* 2010

»» Mecanismos de ultrafiltración

TRANSPORTE

Poros ultrapequeños
 $r < 0.5 \text{ nm}$

Poros pequeños
 $r \text{ 4-6 nm}$

Poros grandes
 $r > 20 \text{ nm}$

Luz capilar

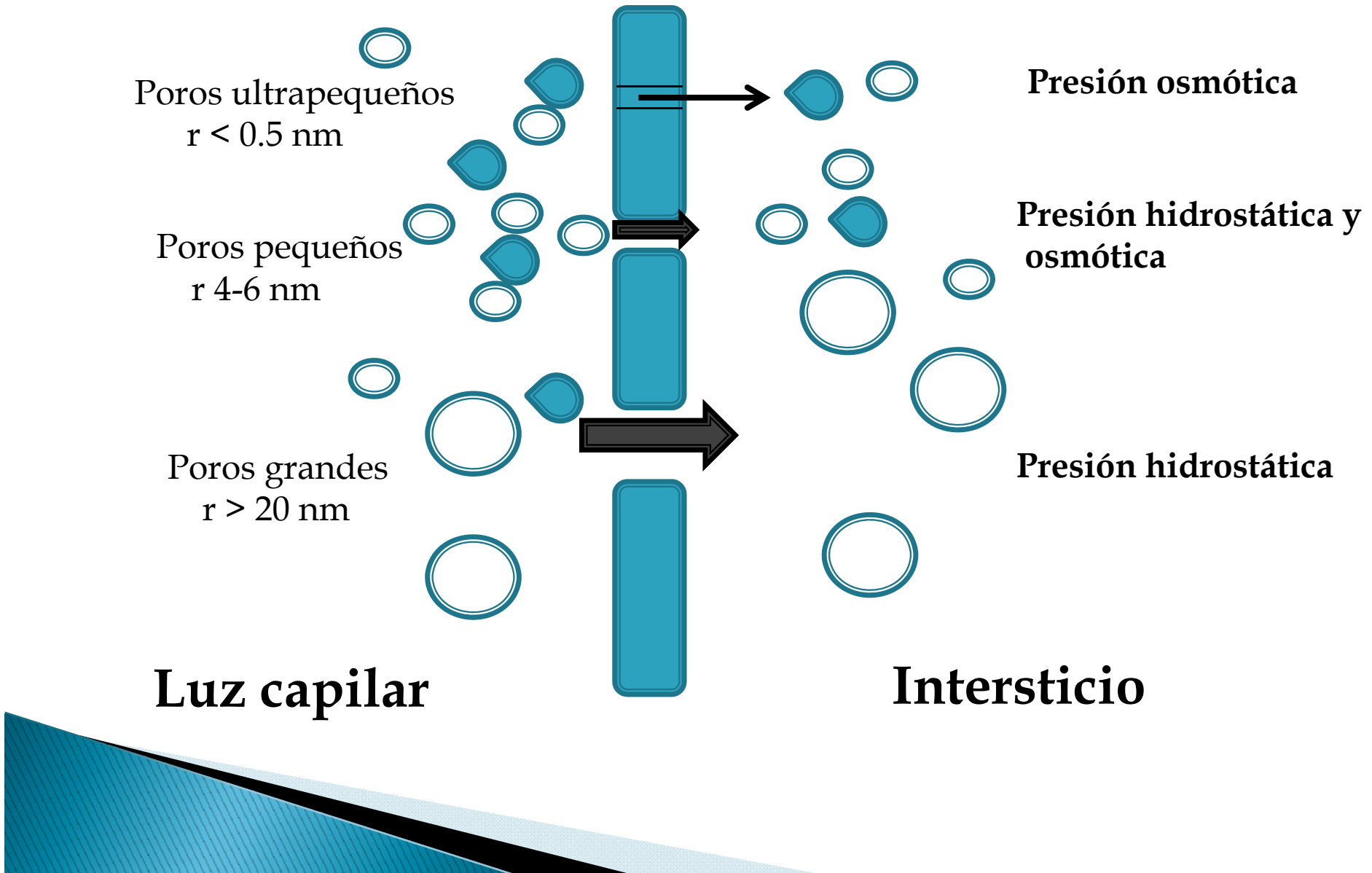
FUERZAS

Presión osmótica

Presión hidrostática y
osmótica

Presión hidrostática

Intersticio



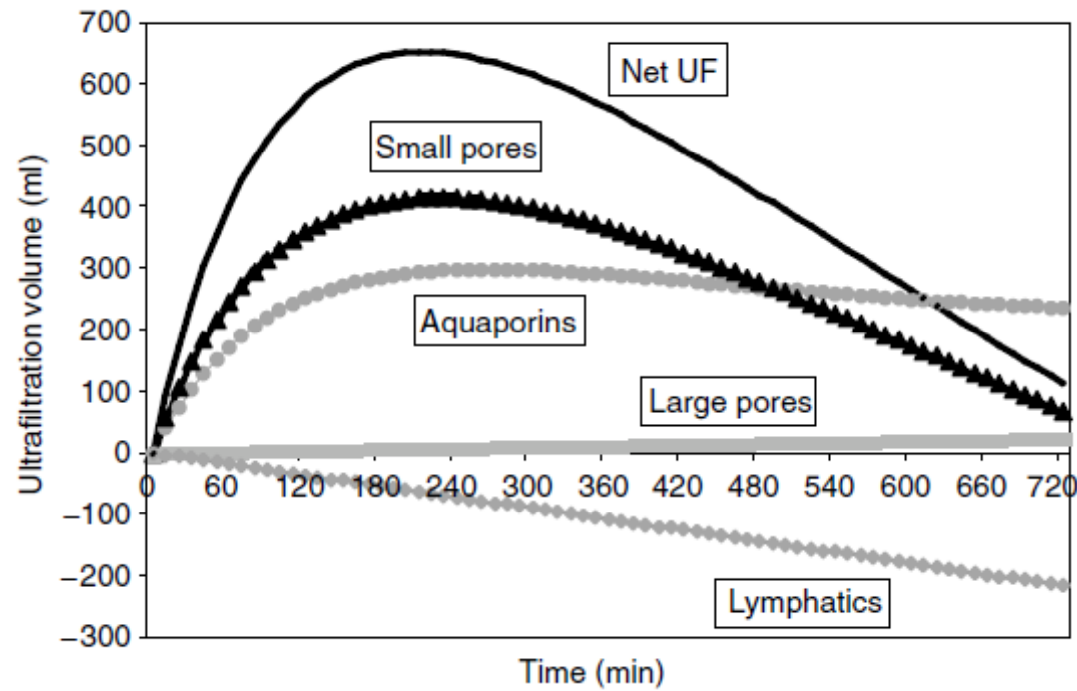
DEFINICIÓN FALLO DE »» ULTRAFILTRACIÓN

Ultrafiltración a las 4 horas inferior a 400 ml en la prueba de permeabilidad peritoneal modificada (con glucosa al 3,86/4,25 %)

Perit Dial Int 2000

»» Componentes del
transporte de agua y como
estudiarlos

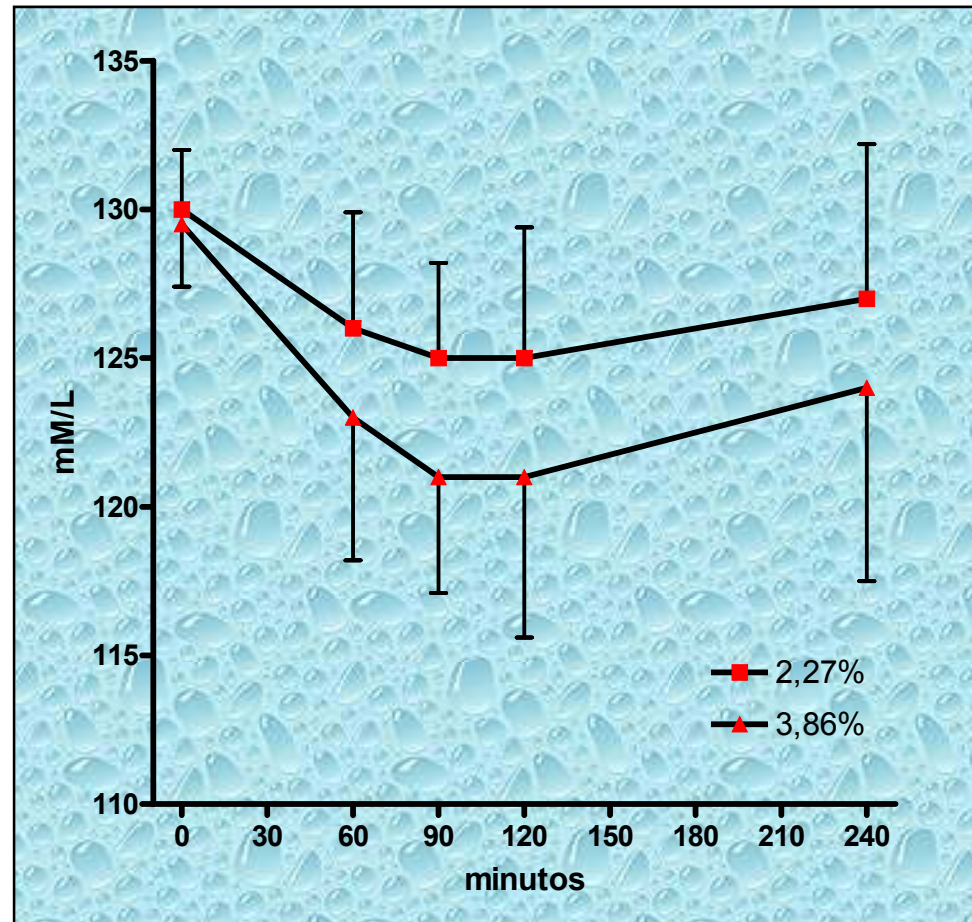
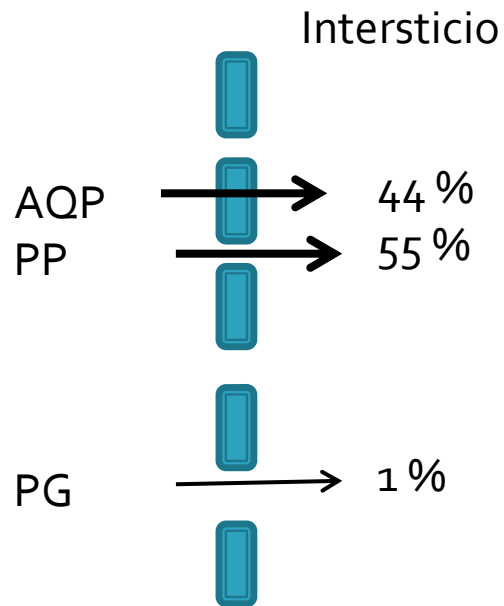
Simulación de la UF con G 3,86%



Davies SJ, Kidney Int 2006; 70: S76-S83

Ultrafiltración con glucosa y cribado de sodio

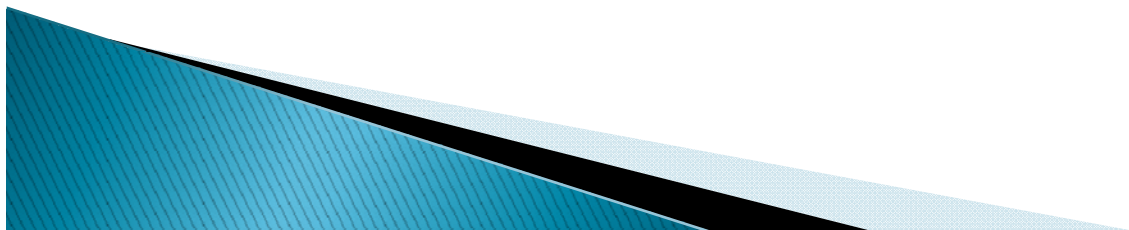
GLUCOSA



Gomes AM Nephrol Dial Transplant 2009; 24:3513

Cálculo de los componentes del transporte de agua

- ▣ Cribado de sodio = Na en líquido infundido – Na en líquido a los 60 min
- ▣ UFPP = eliminación de sodio
(Volumen LD x Na d /Na p)
- ▣ TAL = UF total – UFPP
TAL corregido= UF total (60') + 15-0,92 x UFPP (Venturoli 2005)
15 ml= 18 (abs.linfática 60')- 3 ml(UF poros grandes)



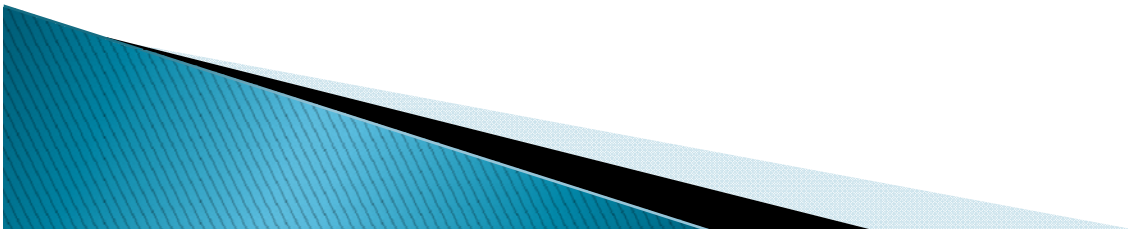
Cálculo de la conductancia osmótica de la glucosa (ml/min/mmHg)

$$\text{COG} = (V_{3,86} - V_{1,36} / (19,3 (G_{3,86} - G_{1,36})60)) \cdot 1,7$$

V volumen drenado al acabar cada miniPEP

G concentración de G (mmol/l) antes de la infusión

G=G (mg/dl) tiempo 0 /18

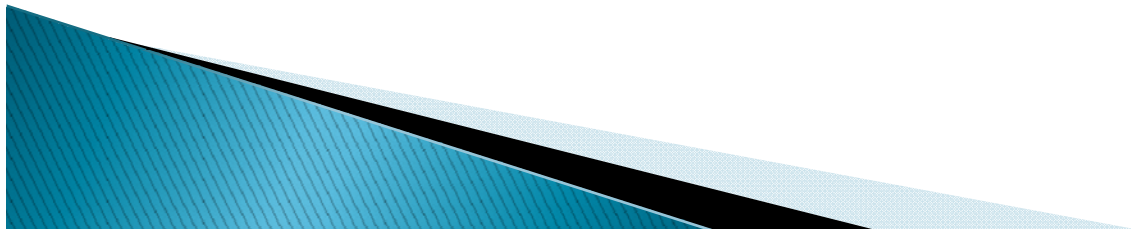




Tipos de fallo de UF

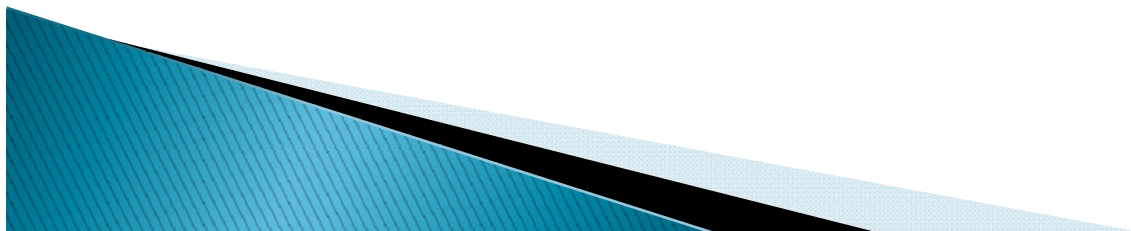
Tipos de fallo de UF

- ▶ Según el momento de aparición
 - Incidente
 - Prevalente
- ▶ Según el mecanismo del fallo de UF
 - Aumento de vascularización
 - Adherencias, esclerosis peritoneal
 - Aumento de reabsorción linfática
 - Déficit de aquaporinas



Fallo de ultrafiltración incidente

- ▶ Incidencia variable. Como media, 10%
- ▶ Manejo fácil si los pacientes tienen diuresis conservada. Posibilidad de utilizar diuréticos
- ▶ Un porcentaje de ellos recuperan la capacidad de ultrafiltración (CHUAC al año 42%)
- ▶ Los que no recuperan pueden tener asociados factores inflamatorios o genéticos



Fallo incidente de UF

Epidemiología

TABLE 1
Clinical Determinants of Peritoneal Transport Rate

Reference	Sample size	Determinant
Churchill <i>et al.</i> , 1998 (28)	606	Old age, male sex, diabetes, hypoalbuminemia
Davies, 2004 (29)	574	Male sex, high residual urine volume
Rumpsfeld <i>et al.</i> , 2004 (30)	3188	Old age, Maori and Pacific Islander ethnicity, normal BMI
Gillerot <i>et al.</i> , 2005 (31)	152	Comorbidity, hypoalbuminemia, diabetes, old age, ACE inhibitor or ARB
Clerbaux <i>et al.</i> , 2006 (32)	72	Diabetes, BSA, ACE inhibitor

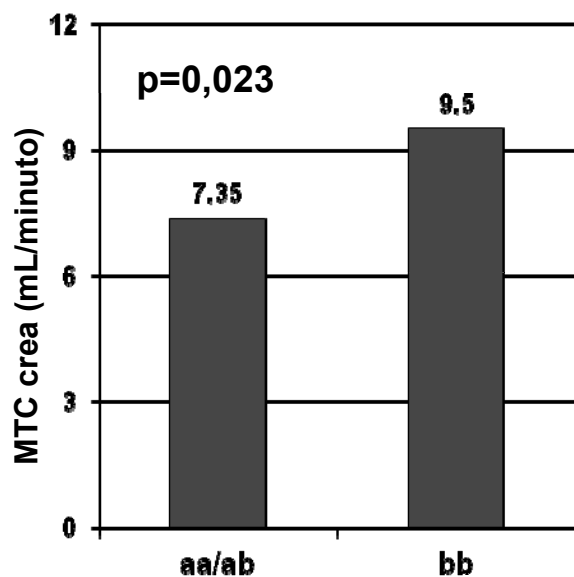
BMI = body mass index; ACE = angiotensin converting-enzyme; ARB = angiotensin II receptor blocker; BSA = body surface area.

Kim. *Perit Dial Int* 2009; 29 (supl. 2): S123

Fallo incidente de UF

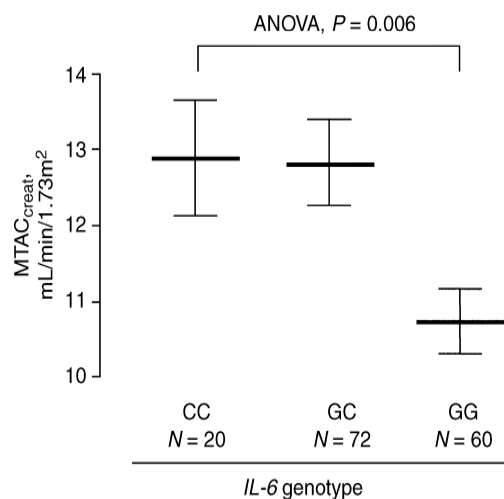
Asociación con polimorfismos genéticos

Polimorfismo gen eNOS



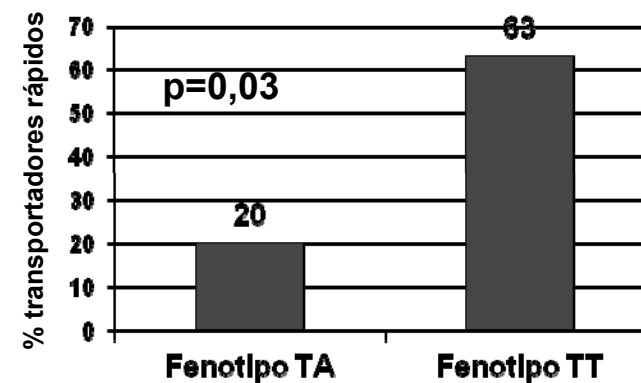
Woag TY et al. *Am J Kidney Dis* 2003; 42: 781

Polimorfismo gen -174G/C IL6



Guillerot et al. *Kidney Int* 2005; 67: 2477

Polimorfismo gen -374T/A receptor AGE



Maruyama et al. *Ther Apher Dial* 2007; 11: 301

El fallo precoz de UF se asocia a aumento de superficie vascular y, en menor medida, a mayor reabsorción linfática

Table 2 | A comparison between patients without UFF (Group I – non-UFF) and patients with UFF (Group I – UFF) treated for less than 2 years, matched for PD duration and age

	Group I (non-UFF)	Group I (UFF)
→ MTAC _{creat} (ml/min)	8.9 (2.5–15.4)	12.2 (5.7–18.6) ^a
→ GA (%)	55 (36–75)	71 (45–81) ^c
→ ELAR (ml/min)	1.4 (0.1–3.3)	2.2 (0.4–5.0) ^b
→ TCUF (ml)	971 (377–1940)	734 (21–1303) ^c
TCUF ₀₋₆₀ (ml)	411 (159–746)	393 (114–883)
SPT ₀₋₆₀ (ml)	268 (71–605)	264 (77–666)
→ FWT ₀₋₆₀ (ml)	168 (48–375)	127 (36–217) ^b
→ FWTC ₀₋₆₀ (%)	42 (13–63)	32 (14–62)
SPTC ₀₋₆₀ (%)	58 (37–87)	68 (38–83)
→ LpA (ml/min/mmHg)	0.10 (0.05–0.32)	0.10 (0.01–0.16)
→ σ	0.045 (0.037–0.054)	0.045 (0.033–0.054)
→ OC (μ l/min/mmHg)	4.5 (2.9–13.4)	4.7 (2.1–7.1)

ELAR, effective lymphatic absorption rate; FWT₀₋₆₀, free water transport within the first hour; FWTC₀₋₆₀, contribution of free water transport within the first hour to the total ultrafiltration; GA, glucose absorption; LpA, ultrafiltration coefficient; MTAC_{creat}, mass transfer area coefficient of creatinine; OC, osmotic conductance to glucose; PD, peritoneal dialysis; SPT₀₋₆₀, small pore fluid transport within the first hour; SPTC₀₋₆₀, contribution of small pore fluid transport within the first hour to the total ultrafiltration; σ , reflection coefficient for glucose; TCUF, transcapillary ultrafiltration; TCUF₀₋₆₀, transcapillary ultrafiltration within the first hour; UFF, ultrafiltration failure. ^a $P \leq 0.05$, ^b $P \leq 0.01$, ^c $P \leq 0.001$.

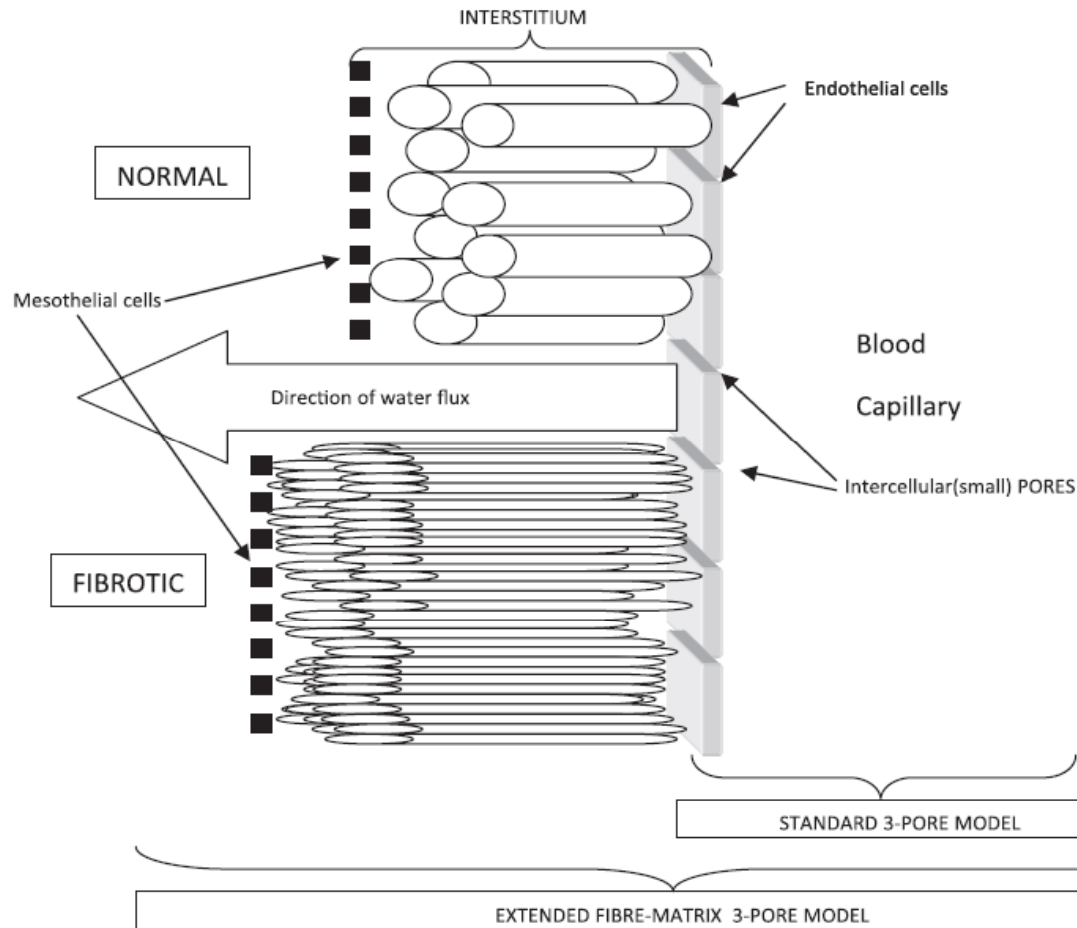
Cambios en la membrana peritoneal en el tiempo

Fallo adquirido de UF Posibles vías patogénicas

- **Aumento del transporte de pequeños solutos**
 - Aumento de la superficie capilar disponible (poros pequeños)
 - Vasodilatación
 - Aumento en el nº de capilares perfundidos
 - Angiogénesis
- **Disminución, de forma desproporcionada, de la capacidad de UF**
 - Pérdida de superficie peritoneal (disminución transporte)
 - “Cegado” de vías de transporte, reduciendo la eficacia osmótica de la glucosa (ej. pérdida de aquaporinas)
 - Aumento selectivo de resistencia de la membrana a la transferencia de fluido: Fibrosis intersticial



Fallo adquirido de UF de acuerdo al modelo de de tres poros extendido



SUMA DE EFECTOS

	D/P Crea	UF
↑Superficie Capilar	↑↑	↓↓
Fibrosis intersticial	↓	↓↓
Cegado vascular (AQ)	=↓	↓↓
EFECTO NETO	↑/↑↑	↓↓↓↓

El fallo adquirido de UF afecta de manera difusa al transporte de agua

Table 1 | A comparison between peritoneal solute transport, fluid kinetics, and determinants of TCUF between Group I (PD duration <24 months), Group II (PD duration 24–60 months), and Group III (PD duration >60 months)

	Group I (UFF)	Group II	Group III	Overall P-value
Number of patients	22	14	14	
PD duration	8 (1–23)	43 (32–59)	96 (61–154)	
<i>Solute and fluid transport parameters after 4 h</i>				
MTAC _{creat} (ml/min)	12.2 (5.7–18.6)	13.3 (9.5–26.6) ^a	15.0 (7.5–25.3)	0.06
GA (%)	71 (45–81)	73 (64–90)	73 (50–84)	0.28
ELAR (ml/min)	2.2 (0.4–5.0)	2.4 (1.0–6.6)	1.7 (0.3–5.0) ^b	0.05
→ TCUF (ml)	734 (21–1303)	742 (523–1310)	625 (265–1386) ^{c,d}	0.01
<i>Water transport during the first hour</i>				
→ TCUF _{0–60} (ml)	393 (114–883)	365 (256–850)	273 (129–431) ^{c,d}	0.01
→ SPT _{0–60} (ml)	267 (77–666)	247 (75–683)	199 (61–345) ^{c,d}	0.01
→ FWT _{0–60} (ml)	127 (36–217)	119 (40–285)	73 (55–149) ^{c,d}	0.02
FWTC _{0–60} (%)	32 (14–62)	32 (2–65)	27 (13–45) ^{c,d}	0.01
SPTC _{0–60} (%)	68 (38–83)	68 (33–98)	73 (55–87)	0.11
<i>Determinants of TCUF</i>				
LpA (ml/min/mmHg)	0.10 (0.01–0.16)	0.11 (0.05–0.21)	0.08 (0.03–0.19) ^b	0.05
σ	0.045 (0.033–0.054)	0.042 (0.032–0.051)	0.042 (0.036–0.053)	0.31
→ OC (μl/min/mmHg)	4.7 (2.1–7.1)	4.6 (2.0–10.6)	3.2 (1.3–7.9) ^b	0.05

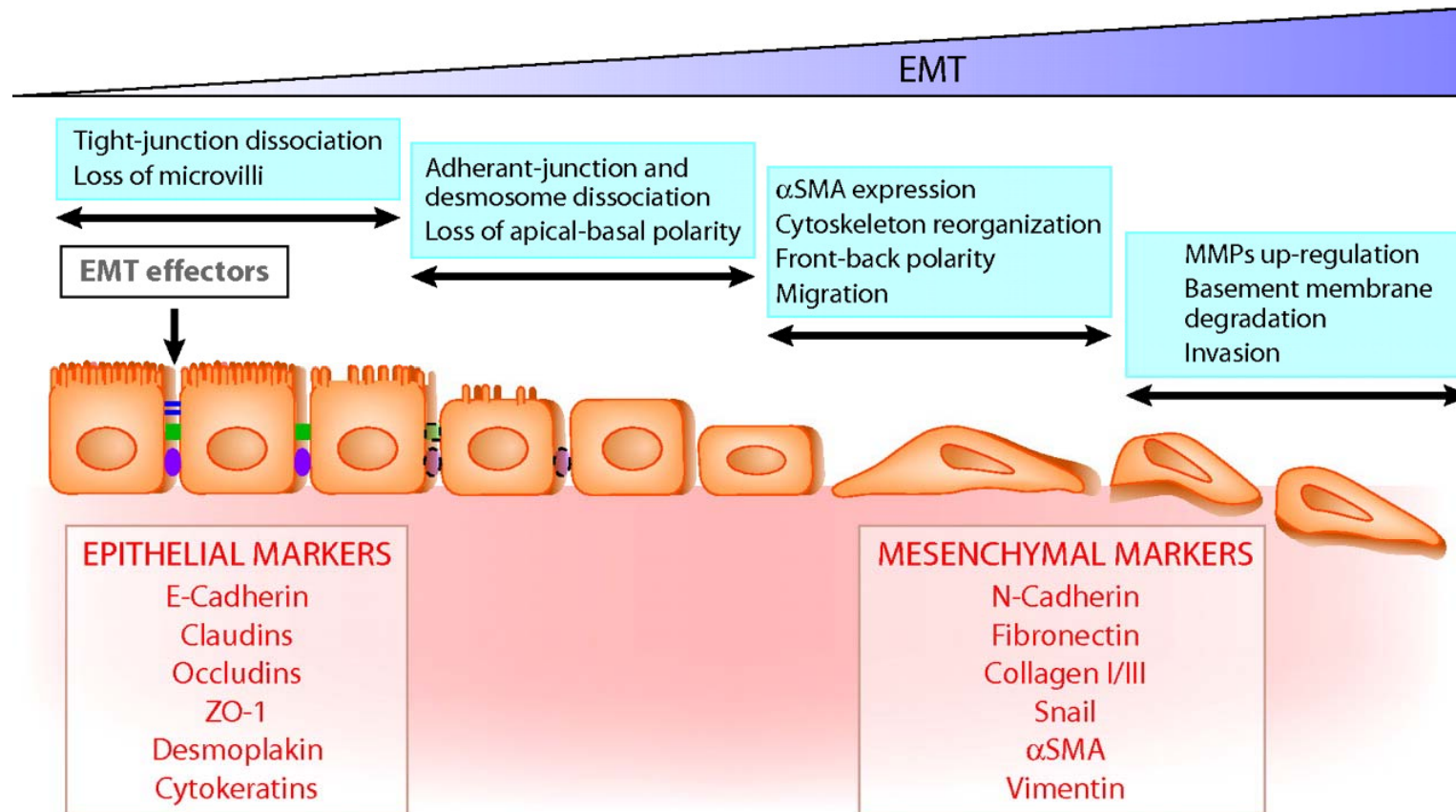
ELAR, effective lymphatic absorption rate; FWT_{0–60}, free water transport within the first hour; FWTC_{0–60}, contribution of free water transport within the first hour to the total ultrafiltration; GA, glucose absorption; LpA, ultrafiltration coefficient; MTAC_{creat}, mass transfer area coefficient of creatinine; OC, osmotic conductance to glucose; PD, peritoneal dialysis; SPT_{0–60}, small pore fluid transport within the first hour; SPTC_{0–60}, contribution of small pore fluid transport within the first hour to the total ultrafiltration; σ, reflection coefficient for glucose; TCUF, transcapillary ultrafiltration; TCUF_{0–60}, transcapillary ultrafiltration within the first hour.

^aGroup I vs group II, $P < 0.06$; ^bGroup II vs Group III, $P < 0.05$; ^cGroup II vs Group III, $P < 0.01$; ^dGroup I vs Group III, $P < 0.01$.

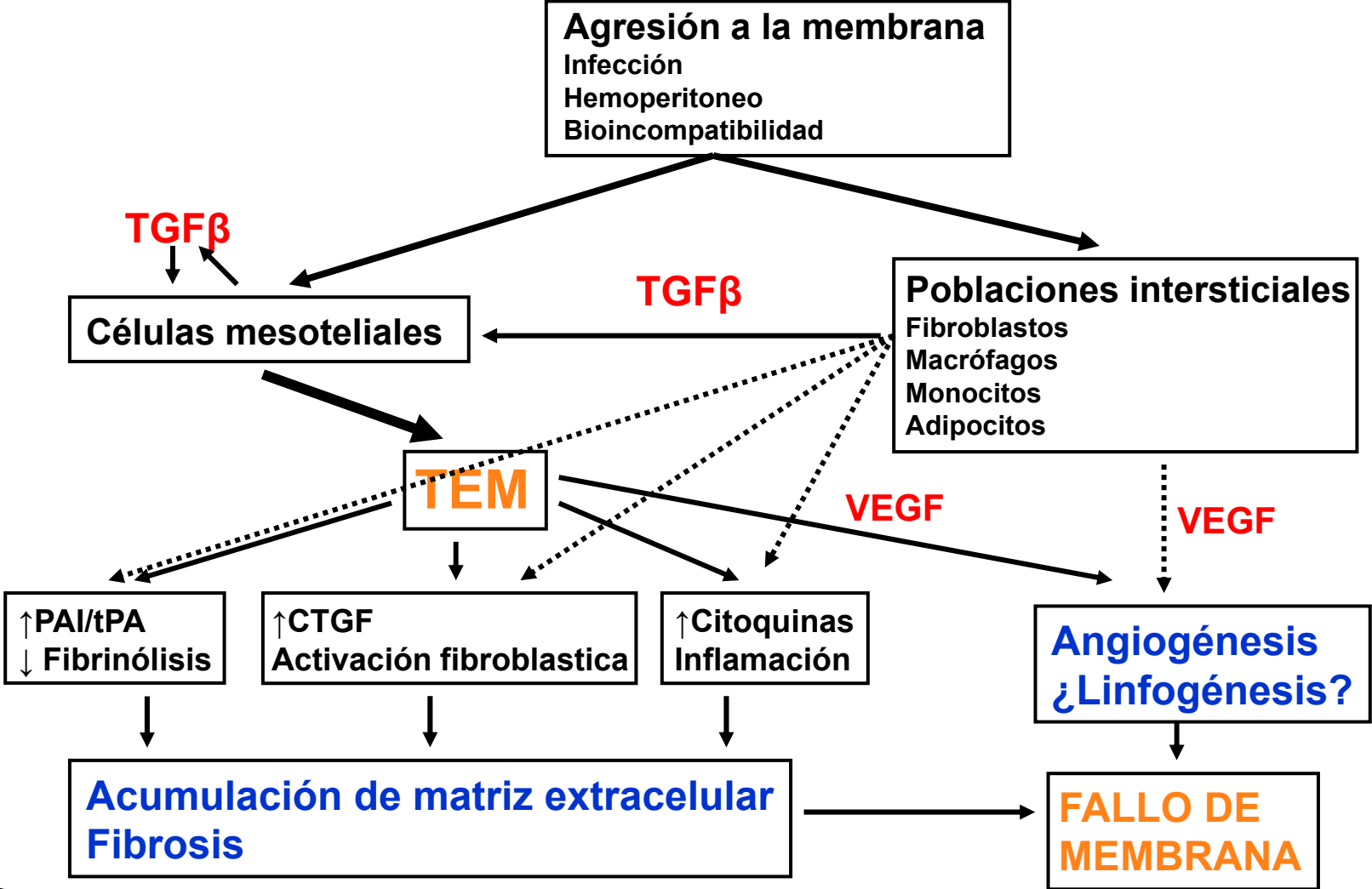
Median values and ranges are given.

Patogenia del fallo adquirido de UF

Transición epitelio-mesenquimal y sus marcadores



La DP y sus interurrencias son los factores esenciales en el deterioro del peritoneo como membrana de diálisis

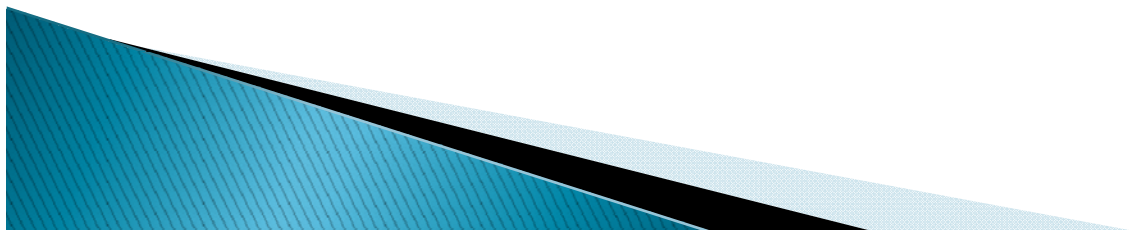


Modif. de Selgas et al. Nephrol, Dial & Transplant 2006; 21 (supl. 2): 2

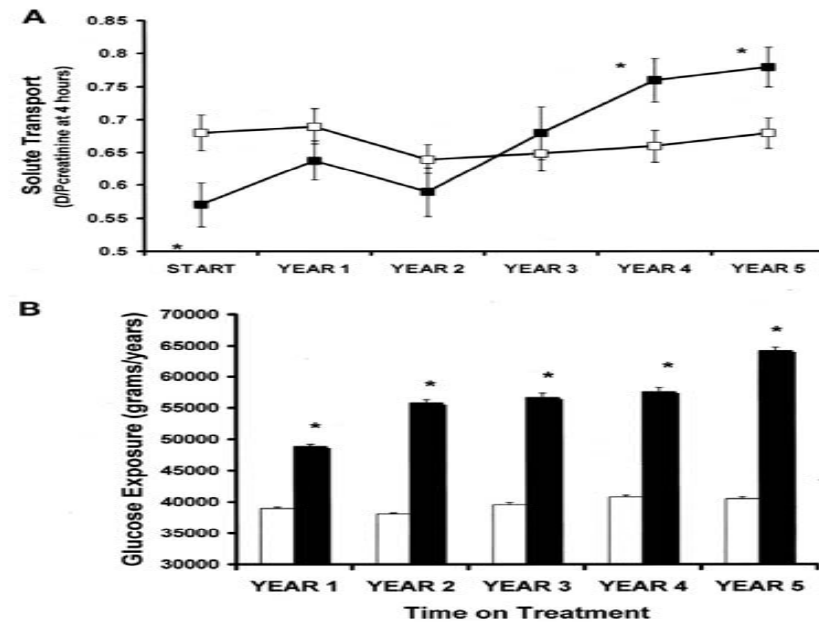
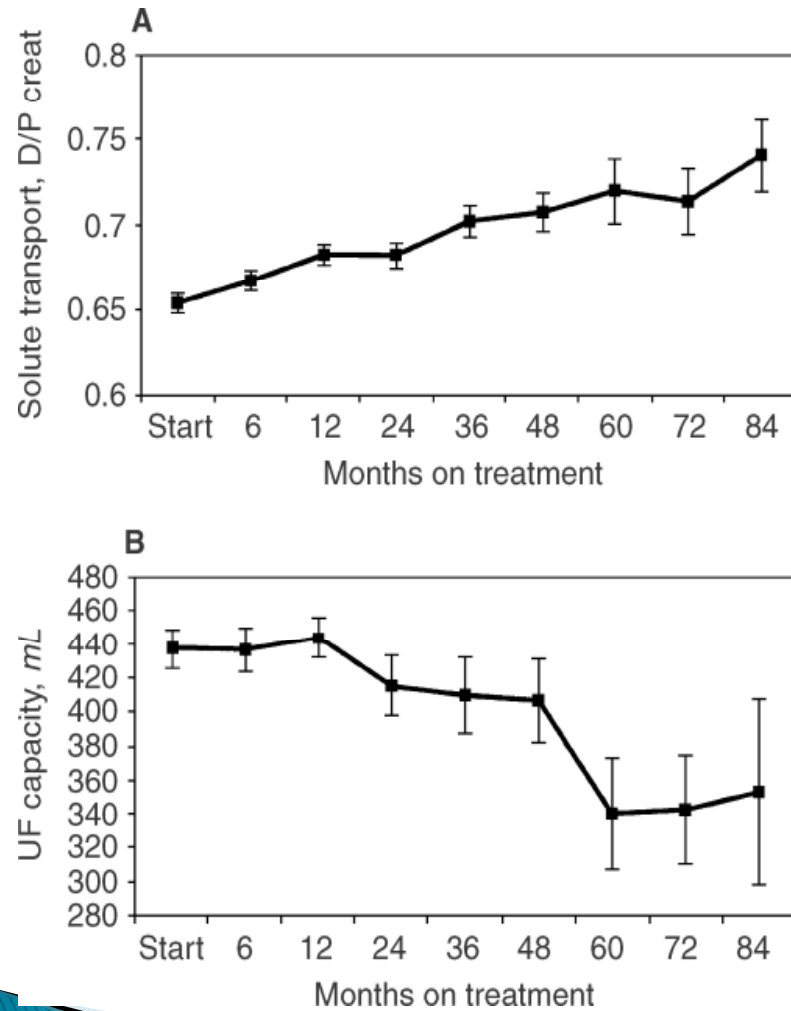
Fallo adquirido de UF

Papel de las infecciones peritoneales

- Efecto obvio de las peritonitis catastróficas
 - Agente: hongos, micobacterias, entéricas
 - Tórpidas, refractarias y mal manejadas
- Efecto más dudoso de una alta frecuencia de peritonitis no complicadas



La permeabilidad tiende a aumentar (y la capacidad de UF a disminuir) con el tiempo en DP



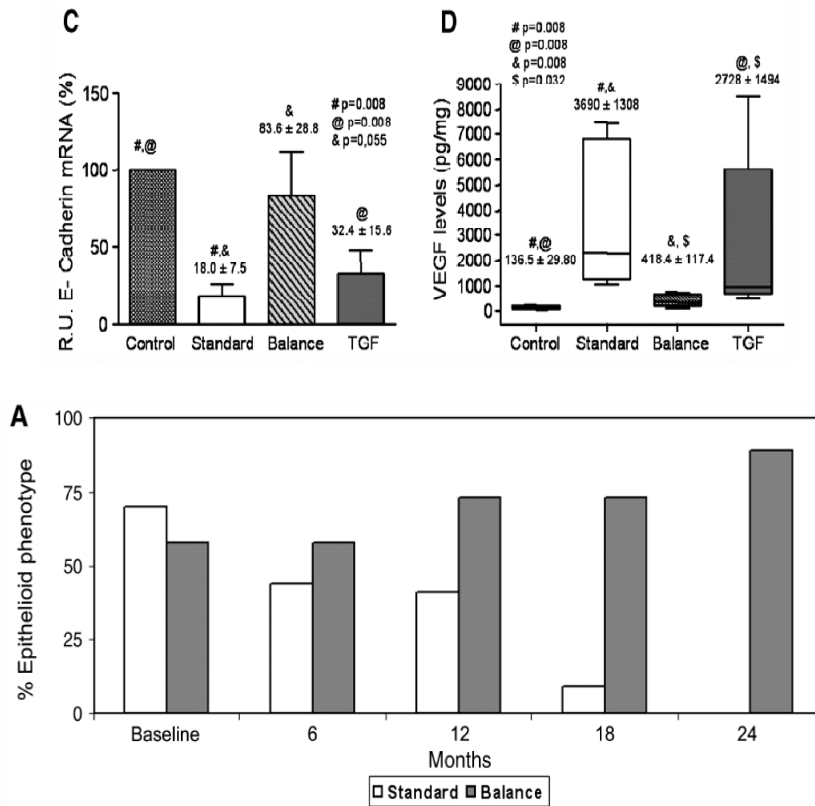
C

Number	Start	Year 1	Year 2	Year 3	Year 4	Year 5
Median	0	0	0	0	0	0.5
Group 1	0.5	1	1	1	1	2
Group 2						
Mann-Whitney	.081	.025	.034	.023	.06	.074

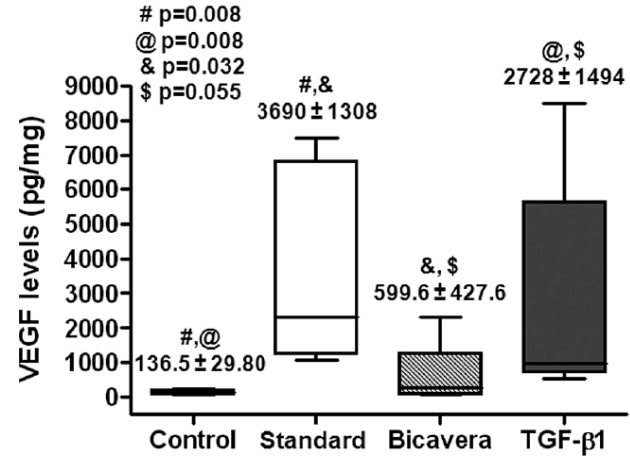
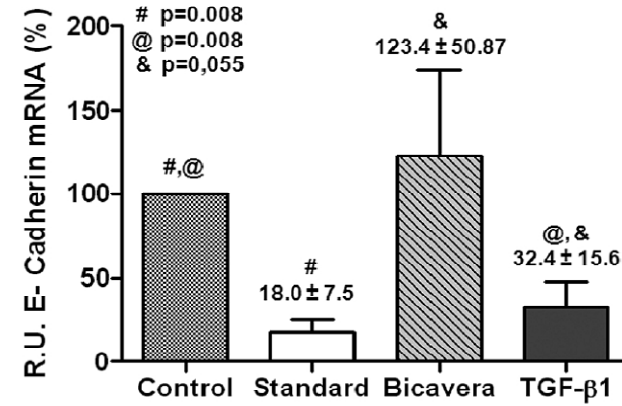
Davies *J Am Soc Nephrol* 2001

Davies. *Kidney Int* 2004; 66: 2437

Efecto *in vitro* y *ex vivo* de soluciones biocompatibles sobre TEM



Bajo MA, *Nephrol, Dial & Transplant* 2011, 26: 282



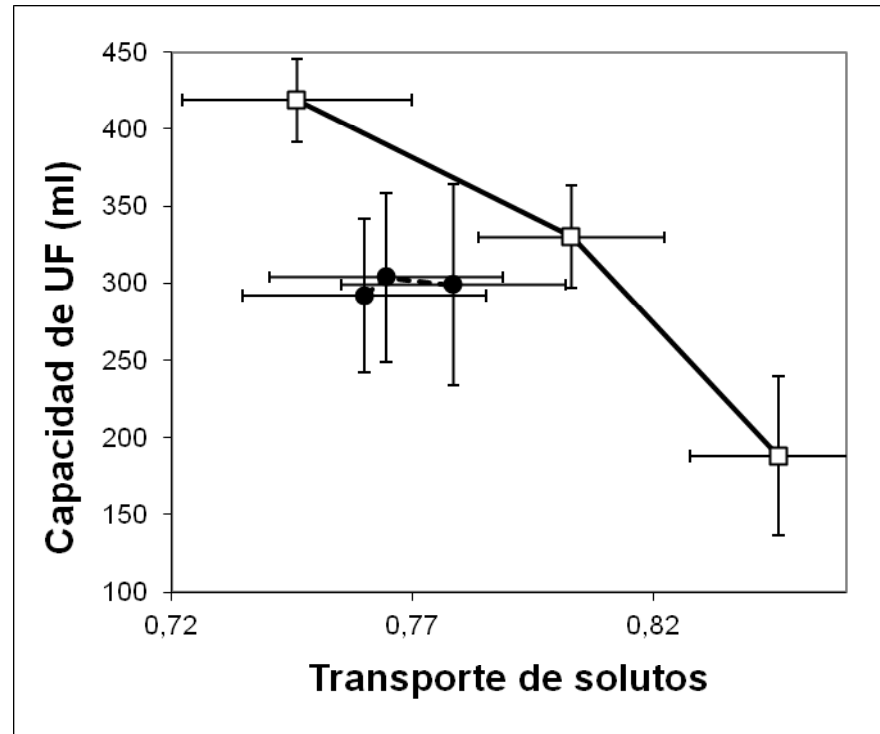
Fernández Perpén, *Perit Dial Int* 2012, 32: 292

Prevención del fallo adquirido de UF

- ▶ Prevención y manejo eficiente de peritonitis
- ▶ Reducción en la carga de glucosa
 - Disciplina dietética
 - Preservación de diuresis y GFR
 - Estrategias ahorradoras de glucosa (icodextrina)
- ▶ Soluciones biocompatibles
- ▶ Modulación farmacológica de la respuesta peritoneal
 - Antagonistas del eje RAA
 - AINEs
 - Experimentales: Sulodexide, benfotiamina, piridoxamina, ácido hialurónico...



Mantenimiento de la capacidad de UF en el tiempo. Efecto de Icodextrina



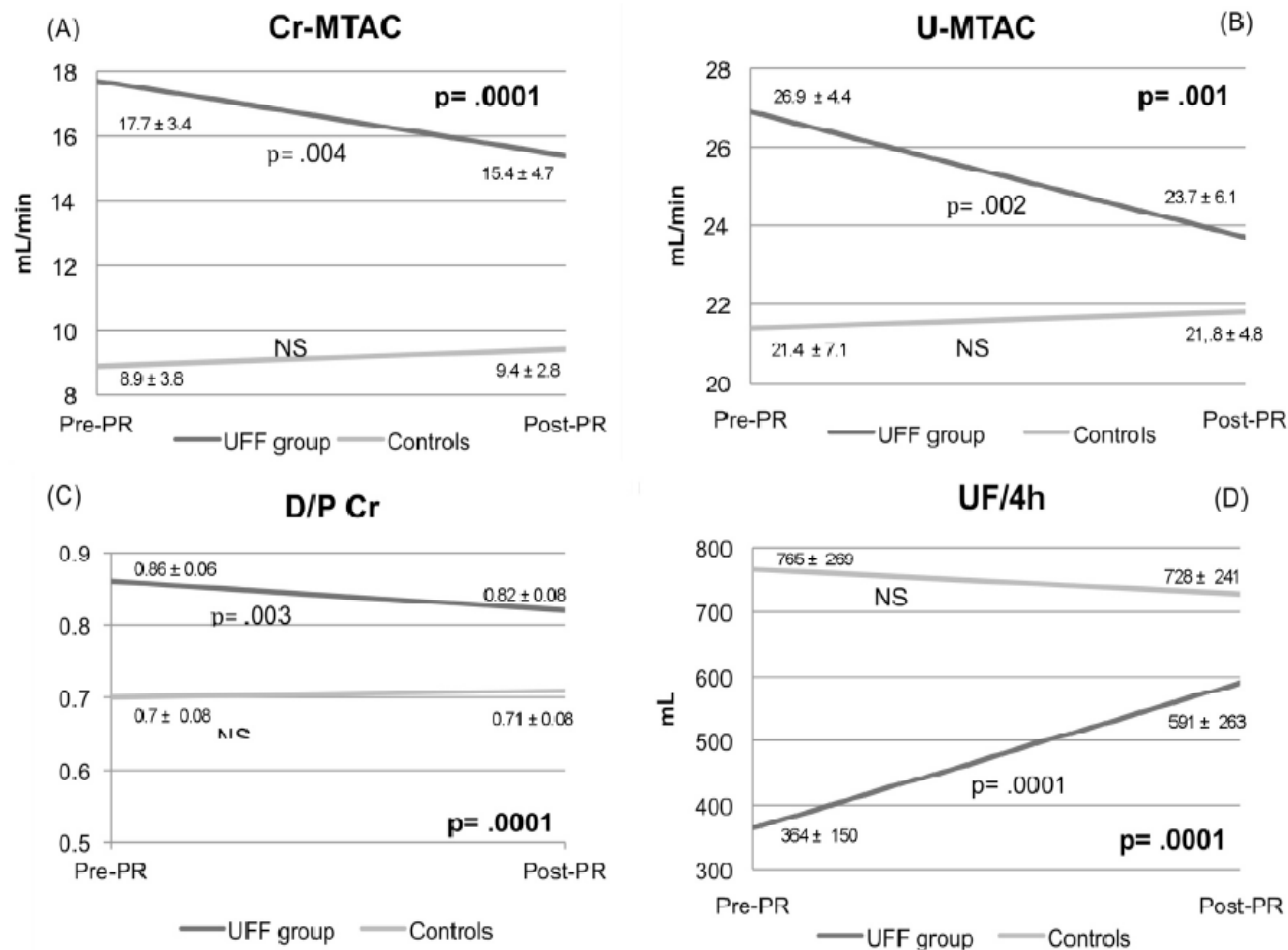
Davies S. *Kidney Int* 2005; 67: 1609

Manejo del paciente con problemas de ultrafiltración



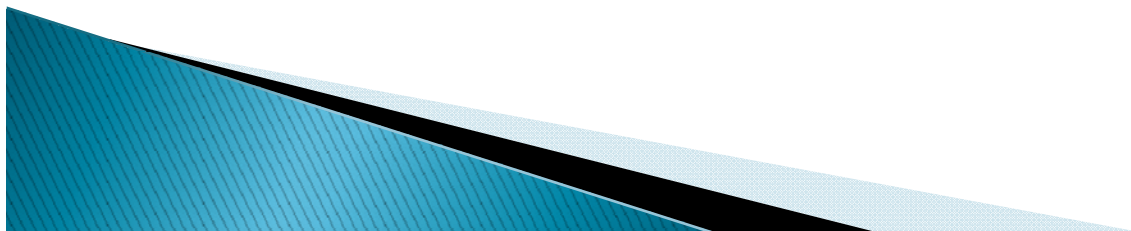
Tratamiento del fallo de UF

Reposo peritoneal y lavados con heparina

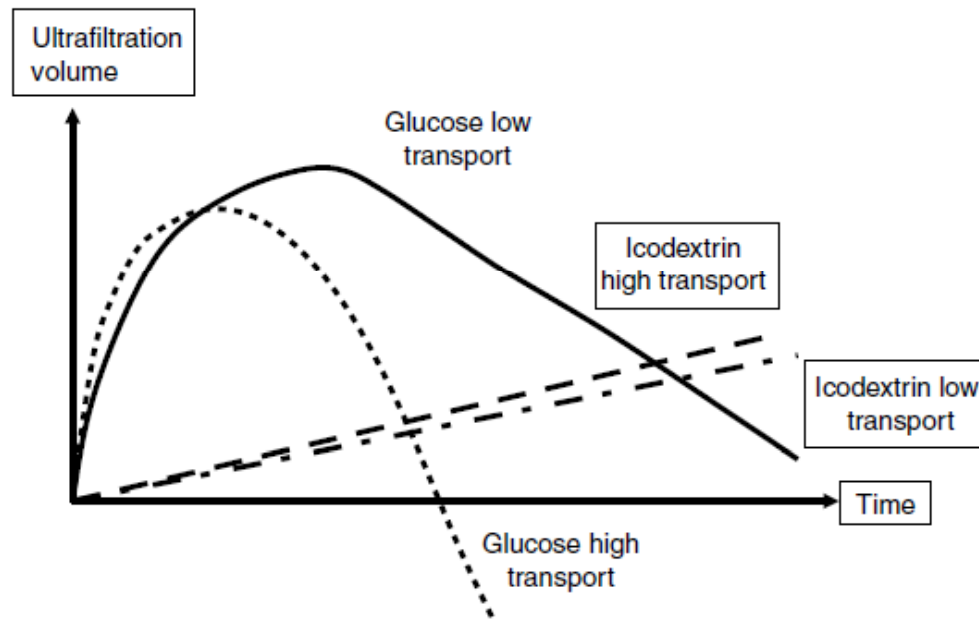


Deficit de UF y rápido transporte

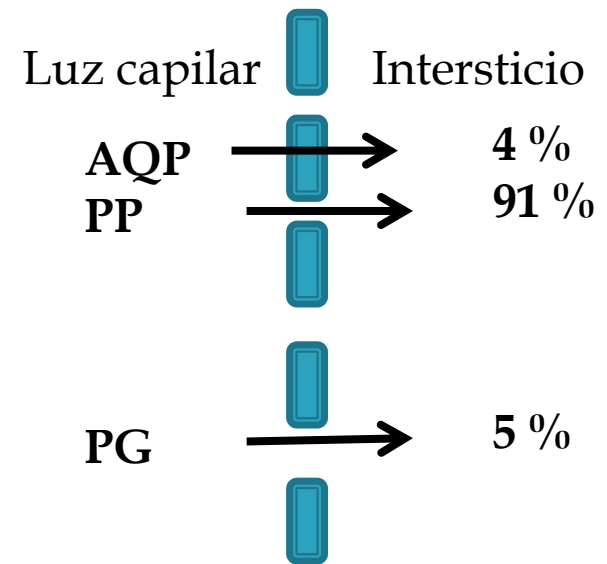
- ▶ La optimización de la diálisis se consigue con DPA que permite realizar cambios de corta permanencia (extracción adecuada de moléculas pequeñas y agua)
- ▶ Cambio diurno con icodextrina que optimiza la UF y compensa la falta de extracción de sodio nocturna
- ▶ Si el paciente tiene diuresis inferior a 200 ml/ 24 horas puede necesitar cambio diurno suplementario



Utilidad de la Icodextrina



Davies SJ, *Kidney Int* 2006; 70: S76-S83



Adaptación Devuyst *Kidney Int.* 2014

Diálisis peritoneal adaptada

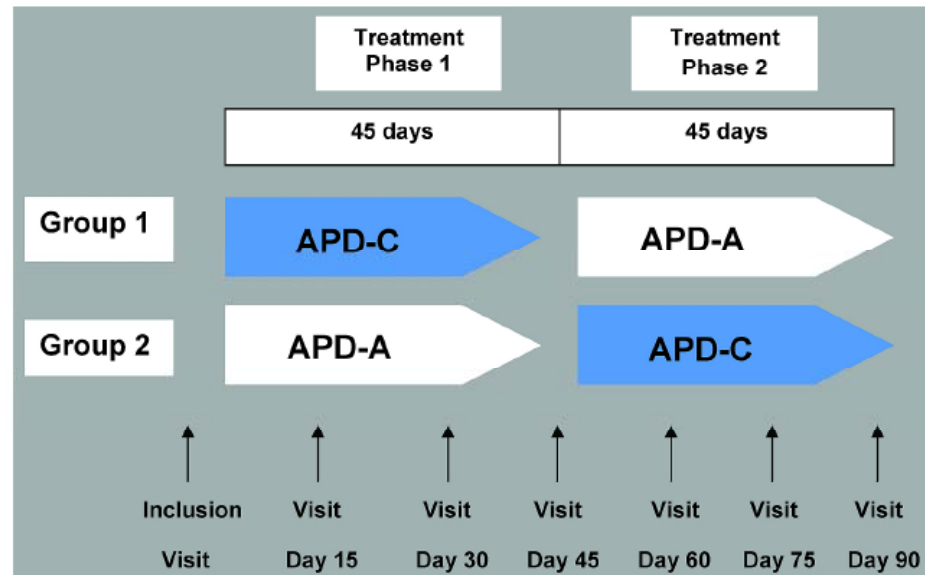
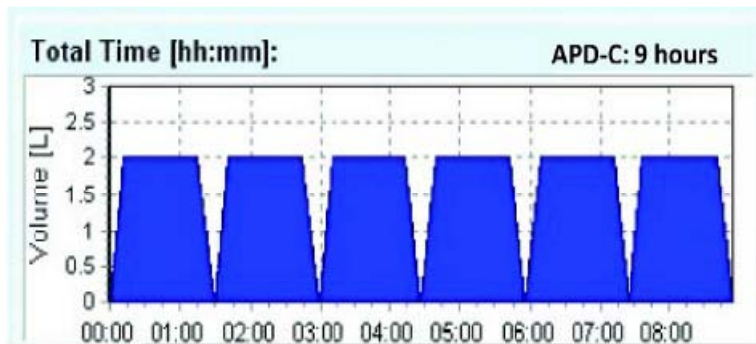
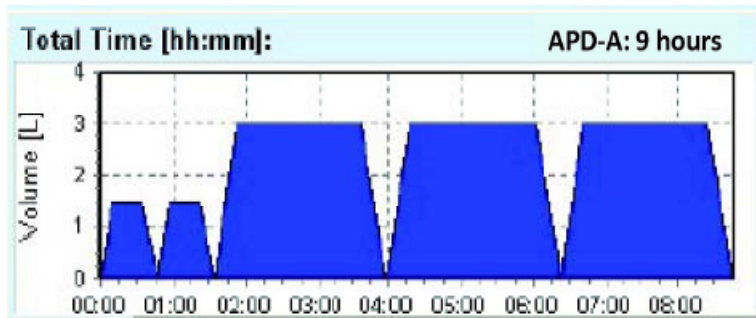


Figure 1 — Flow diagram of the study design. APD-C = conventional automated peritoneal dialysis (APD); APD-A = adapted APD.

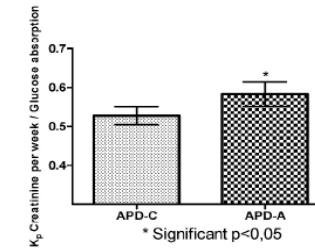
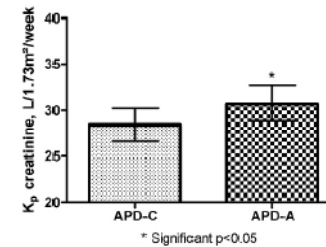
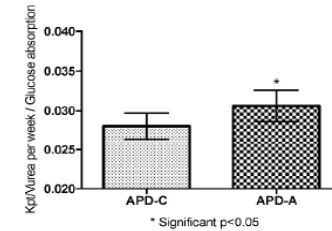
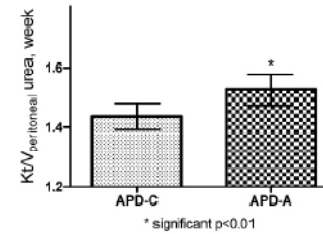
n= 22 pacientes

M. Fischbach , PDI 2011

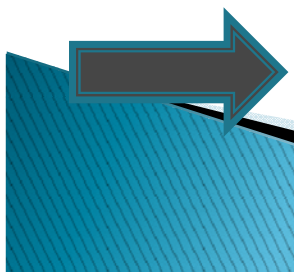
Diálisis peritoneal adaptada

TABLE 2
Mean Blood Pressure at the End of the 45-Day Adapted (APD-A) and Conventional Automated Peritoneal Dialysis (APD-C) Periods

Blood pressure reading	Dialysis regimen		<i>p</i> Value
	APD-C	APD-A	
Systolic	144.3±18.9	139.0±20.2	0.022
Diastolic	83.3±15.4	79.7±14.4	0.016
Overall	104.7±14.7	100.3±14.4	0.0056

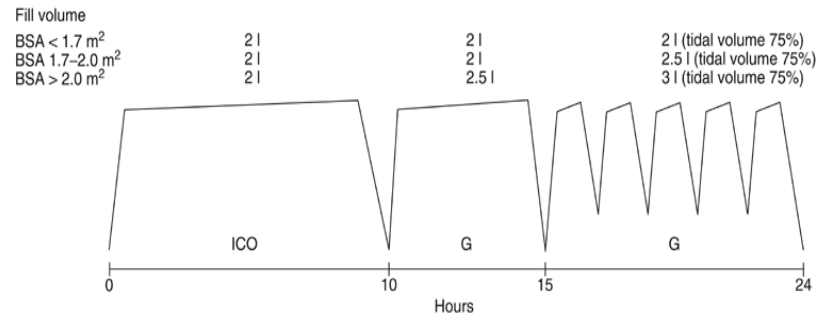


Variable	APD-C (n=19)	APD-A (n=19)	<i>p</i> Value
Urea			
Plasma [P (mmol/L)]	22.34±5.35	21.99±4.69	NS
Dialysate [D (mmol/L)]	10.92±2.47	12.65±2.35	<0.05
D/P	0.526±0.118	0.570±0.135	<0.01
Creatinine			
Plasma [P (μmol/L)]	665.9±184.3	658.8±173.1	NS
Dialysate [D (μmol/L)]	202.0±53.5	215.9±65.8	<0.05
D/P	0.230±0.059	0.327±0.049	<0.05
Dialysate sodium (mmol/L)	126.4±1.4	127.5±1.3	<0.05
Dialysate phosphate (mmol/L)	0.384±0.076	0.425±0.053	<0.05
Drained dialysate per session (L)	15.675±1.497	16.237±1.375	<0.05
Daily ultrafiltration (mL)	656±275.3	743±358.3	<0.01

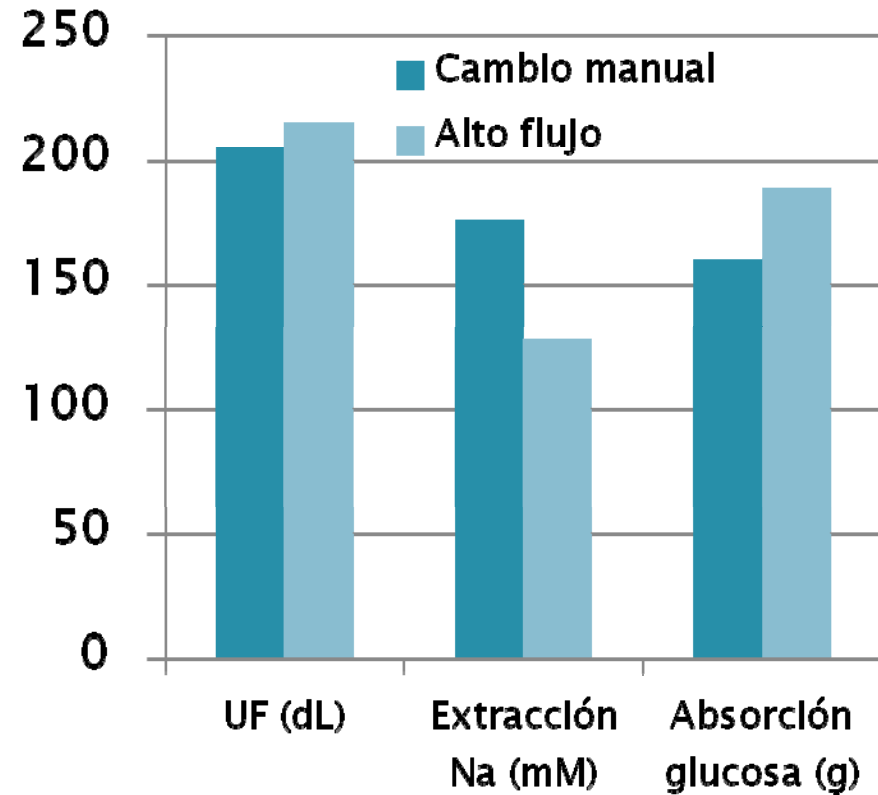
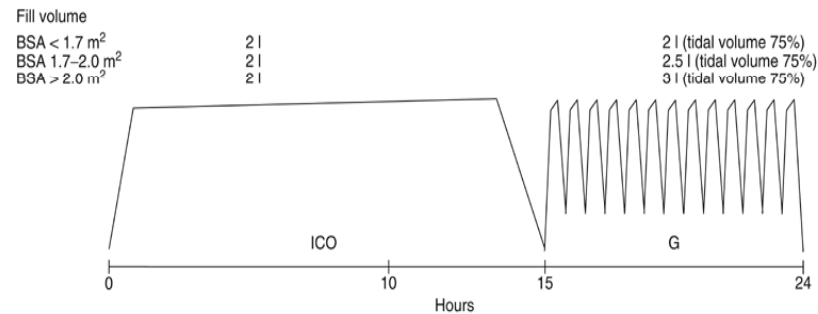


Optimización de UF y extracción de Na en DPA

'Manual exchange' treatment



'High flow' treatment

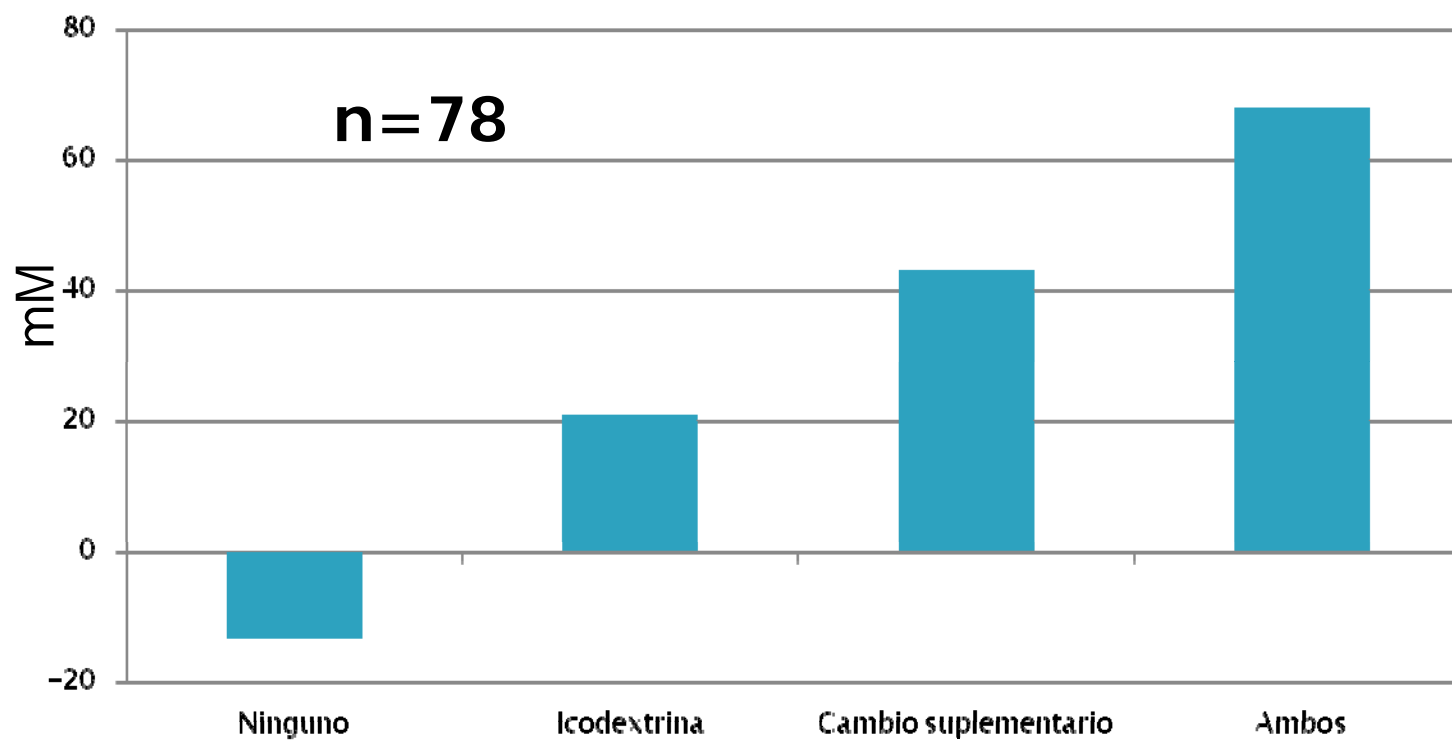


Programación de DPA

Valores diurnos según terapia

		Valor nocturno	Std	1	2	3	4
Standard	14 hr, 2.27% G						
Therapy 1	T _{OPT} , 2.27% G DRY	Ultrafiltración (ml)	-230	183	210	476	574
Therapy 2	7 hr, 2.27% G 7 hr, 2.27% G	Extracción de Na (mEq)	-26	18	22	71	77
Therapy 3	14 hr, 7.5% Icodextrin	Absorción Glucosa (g)	42	33	75	71	90
Therapy 4	T _{OPT} , 2.27% G Rest of the day, 7.5% Icodextrin	Eficiencia UF (ml/min)	-5.4	5.5	2.8	6.7	6.4

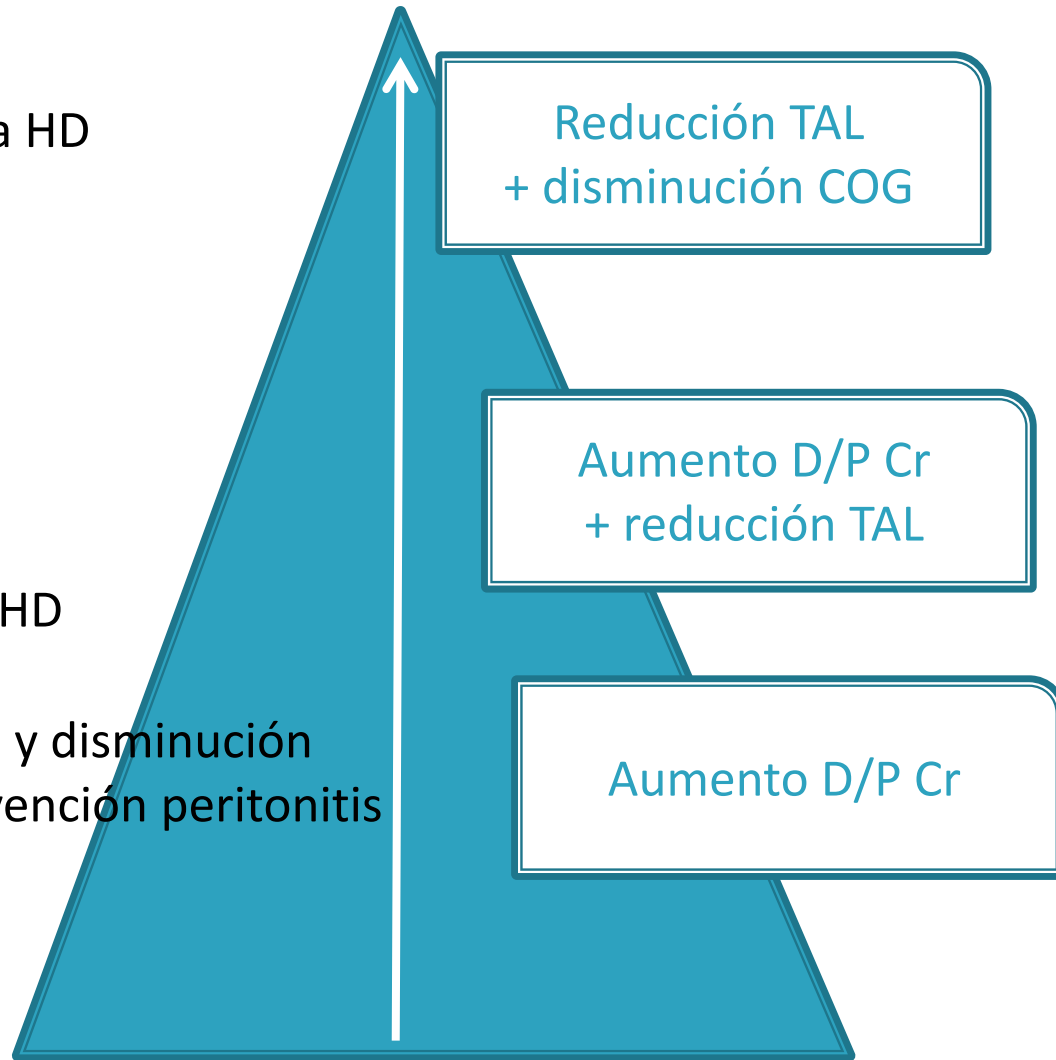
Efecto de poliglucosa y cambio suplementario sobre la extracción diurna de sodio en DPA



Programar transferencia a HD
Tamoxifeno

DPA. Icodextrina
Tamoxifeno?
Se puede usar glucosa
Planificar transferencia a HD

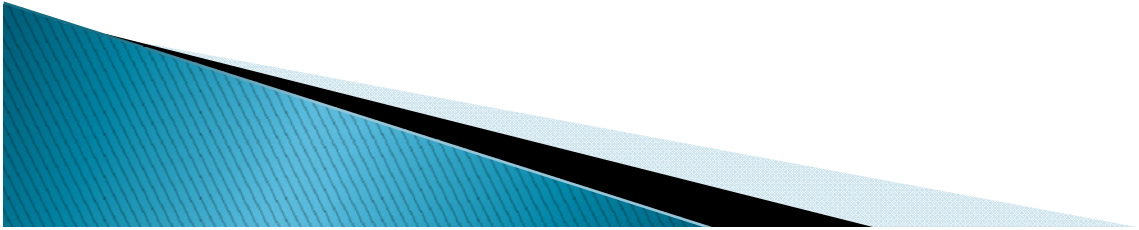
Soluciones con bajos GPD y disminución
de carga de glucosa . Prevención peritonitis
Reposo peritoneal
DPA + Icodextrina



2º CONGRESO DE LA SOCIEDAD GALLEGA DE NEFROLOGIA



Muchas Gracias



PET parameters , diagnosis and prognosis

parameter	result	diagnosis	prognosis
4h dwell UF	< 400 mL	diagnostic of UFF	Variable
D/P creatinine	>0.81 (fast transport)	Type 1	frequent, elective for APD +icodextrin
	< 0.65 (slow transport)	Type 2	Rare
Sodium Dip (Δ DNa)	Decreased < 5 mmol/L	May occur in fast transport due to sodium diffusion	Merged information
		May sign aquaporin dysfunction	Often present in late UFF
Free water transport (60 min dwell)	Moderately decreased	May occur in fast transport	Intermediate sign of lesion
	absolute mL Severely decreased	Signs aquaporin dysfunction and /or Interstitial fibrosis	Severe late UFF Increased risk of sclerosis
	percent % <45% (corrected)		
OC	Decreased	Loss Hydraulic permeability	Increased risk of sclerosis
4h dwell CA125	Decreased (profile)	Signs worse membrane status	Increased risk of sclerosis
4h dwell IL-6	Increased (profile)	Signs local inflammation	

Gentileza Anabela Rodrigues

Mecanismos de Fallo de UF

	UF	D/P	Cribado Na	Reab.linfática	Significado
I	↓	↑	↓	N	↑ superficie/vasos peritonitis
II	↓	↓	↑	N	Adherencias P. esclerosante
III	↓	N	N	↑	Aumento de linfáticos
IV	↓	N	No	N	↓ Aquaporinas