THE ADVANCED TREATMENT OF CHRONIC HEART FAILURE BY PERITONEAL ULTRAFILTRATION

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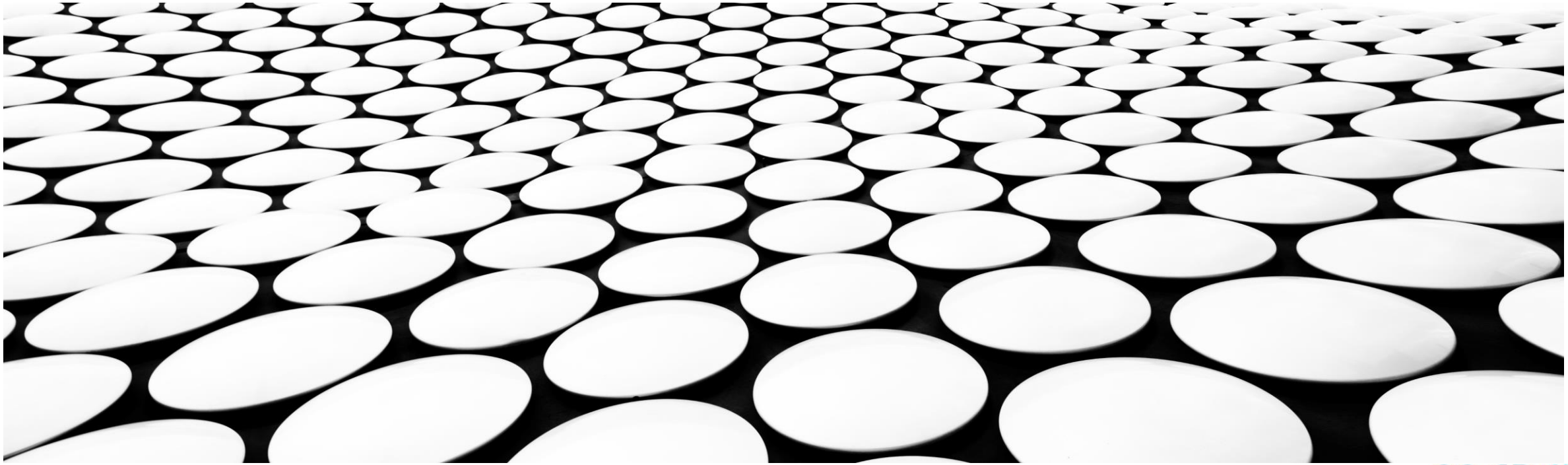
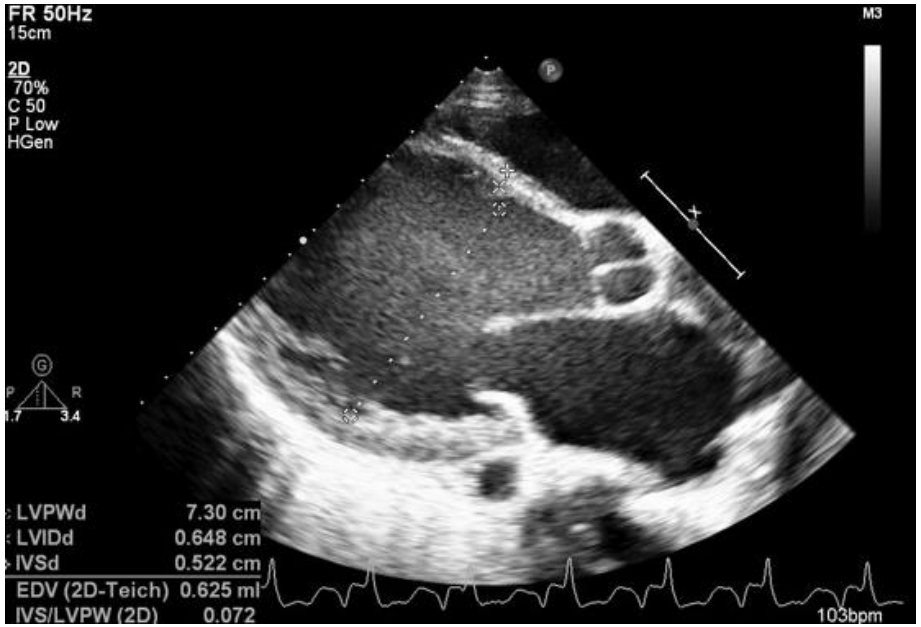


Chronic heart failure (HF)

- a **clinical syndrome** that brings together **cardiac symptoms and signs** resulting from **structural and/or functional abnormalities** of the heart that cause **increased intracardiac pressure and/or inappropriate stroke volume** at rest and/or exertion

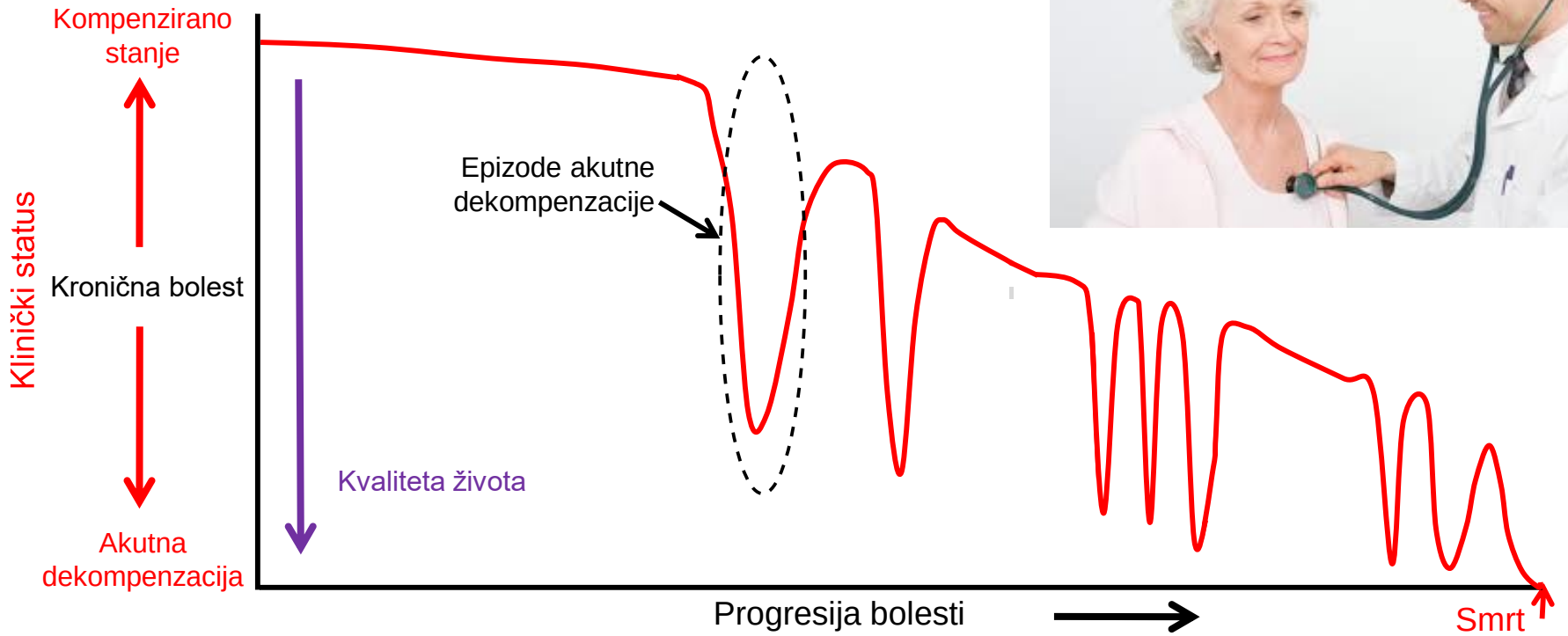


HFA
Heart Failure
Association

2021 ESC HF Guidelines www.escardio.org/guidelines

Epidemiology and natural course of HF

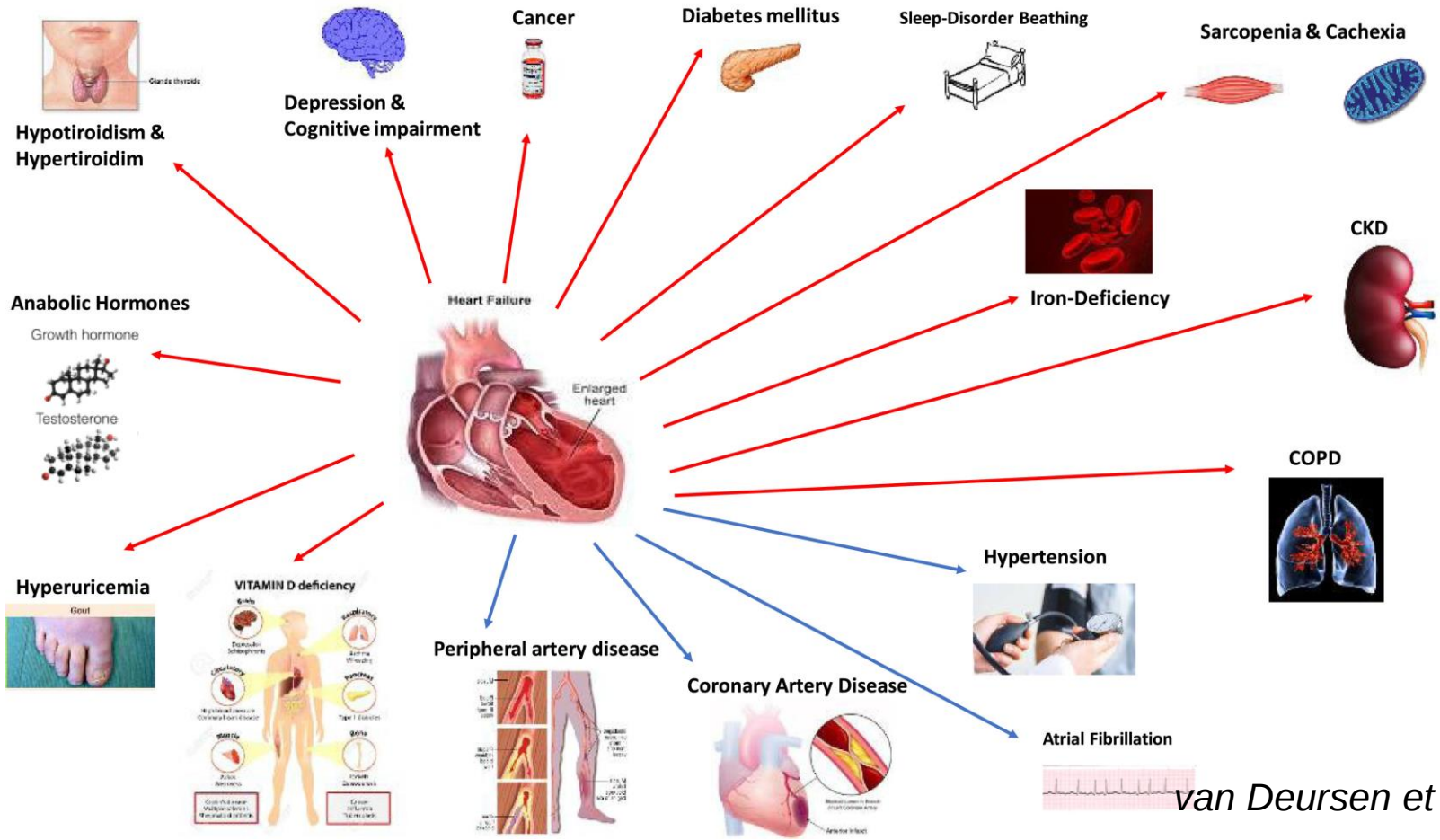
- chronic progressive disease with poor prognosis



Ahmed et al. Am Heart J 2006;151:444–50; Gheorghiade et al. Am J Cardiol 2005;96:11G–17G.

Comorbidities in patients with CHF

- 74% of patients whtih HF in *ESC Heart Failure Pilot Study* reported at least



van Deursen et al. Eur J Heart Fail 2014;16:103–111.

Correale N. et al. Eur J Int Med. 72020; 71: 23-31.

Type of HF and severity of symptoms

Table 3 Definition of heart failure with reduced ejection fraction, mildly reduced ejection fraction and preserved ejection fraction

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF ≤40%	LVEF 41–49%[b]	LVEF ≥50%
	3	–	–	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides[c]

Table 4 New York Heart Association functional classification based on severity of symptoms and physical activity

Class I	No limitation of physical activity. Ordinary physical activity does not cause undue breathlessness, fatigue, or palpitations.
Class II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
Class III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity results undue breathlessness, fatigue, or palpitations.
Class IV	Unable to carry on any physical activity without discomfort. Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased.

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Medical treatment of HF

Table 8 Evidence-based doses of disease-modifying drugs in key randomized trials in patients with heart failure with reduced ejection fraction

	Starting dose	Target dose
ACE-I		
Captopril[a]	6.25 mg *t.i.d.*	50 mg *t.i.d.*
Enalapril	2.5 mg *b.i.d.*	10–20 mg *b.i.d.*
Lisinopril[b]	2.5–5 mg *o.d.*	20–35 mg *o.d.*
Ramipril	2.5 mg *b.i.d.*	5 mg *b.i.d.*
Trandolapril[a]	0.5 mg *o.d.*	4 mg *o.d.*
ARNI		
Sacubitril/valsartan	49/51 mg *b.i.d.*[c]	97/103 mg *b.i.d.*
Beta-blockers		
Bisoprolol	1.25 mg *o.d.*	10 mg *o.d.*
Carvedilol	3.125 mg *b.i.d.*	25 mg *b.i.d.*[e]
Metoprolol succinate (CR/XL)	12.5–25 mg *o.d.*	200 mg *o.d.*
Nebivolol[d]	1.25 mg *o.d.*	10 mg *o.d.*
MRA		
Eplerenone	25 mg *o.d.*	50 mg *o.d.*
Spironolactone	25 mg *o.d.*[f]	50 mg *o.d.*
SGLT2 inhibitor		
Dapagliflozin	10 mg *o.d.*	10 mg *o.d.*
Empagliflozin	10 mg *o.d.*	10 mg *o.d.*
Other agents		
Candesartan	4 mg *o.d.*	32 mg *o.d.*
Losartan	50 mg *o.d.*	150 mg *o.d.*
Valsartan	40 mg *b.i.d.*	160 mg *b.i.d.*
Ivabradine	5 mg *b.i.d.*	7.5 mg *b.i.d.*
Vericiguat	2.5 mg *o.d.*	10 mg *o.d.*
Digoxin	62.5 µg *o.d.*	250 µg *o.d.*
Hydralazine/ Isosorbide dinitrate	37.5 mg *t.i.d.*/20 mg *t.i.d.*	75 mg *t.i.d.*/40 mg *t.i.d.*

life saving therapy

disease modifying drugs

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Advanced forms of HF (2)

- renal dysfunction and **resistance to diuretics** are one of the most common characteristics of patients with advanced HF
- in patients who do not respond to the recommended doubling loop diuretics dose with the accompanying addition of thiazide (or metolazone), it is necessary to **consider the use of continuous ultrafiltration** (slow continuous ultrafiltration, SCUF), **continuous methods of hemodialysis**, and **peritoneal ultrafiltration** / **dialysis** (PUF/ PD) depending on the accompanying volume status, parameters of renal function and electrolyte

Renal replacement therapy should be considered in patients with refractory volume overload and end-stage kidney failure.	IIa	C

Recommendations for the treatment of patients with advanced heart failure

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Renal replacement therapy

- extracorporeal therapy - "myocardial stunning" with a potential long-term impact on the progression of HF
- **potential benefits of peritoneal dialysis (PD):**
- minimal impact on hemodynamics and the absence of additional unfavorable neurohumoral stimulation
- continuous removal of volume load and electrolyte
- better tolerance of dose adjustment of medicinal therapy for HF
- drainage of ascites and reduction of intra-abdominal pressure while improving renal function
- absence of risk of central vascular access and hemodynamic effects of A-V fistula
- psychosocial circumstances, quality of life

Francois K. et al. Blood Purif. 2015; 40: 45-52.

PERITONEAL ULTRAFILTRATION/DIALYSIS IN END-STAGE CHRONIC HEART FAILURE

- Peritoneal ultrafiltration/dialysis (PUF/PD) appears to be a promising supportive long-term therapy of chronic heart failure (CHF) refractory to diuretics in patients with and without chronic kidney disease (CKD)
- The beneficial effects of PD/PUF:
  - improvement in congestive symptoms
  - decrease in numbers and durations of hospitalizations
  - enhanced quality of life
  - decline in cost of care
  - better exercise capacity
- PUF/PD can be used either as palliative therapy or as bridge to transplantation

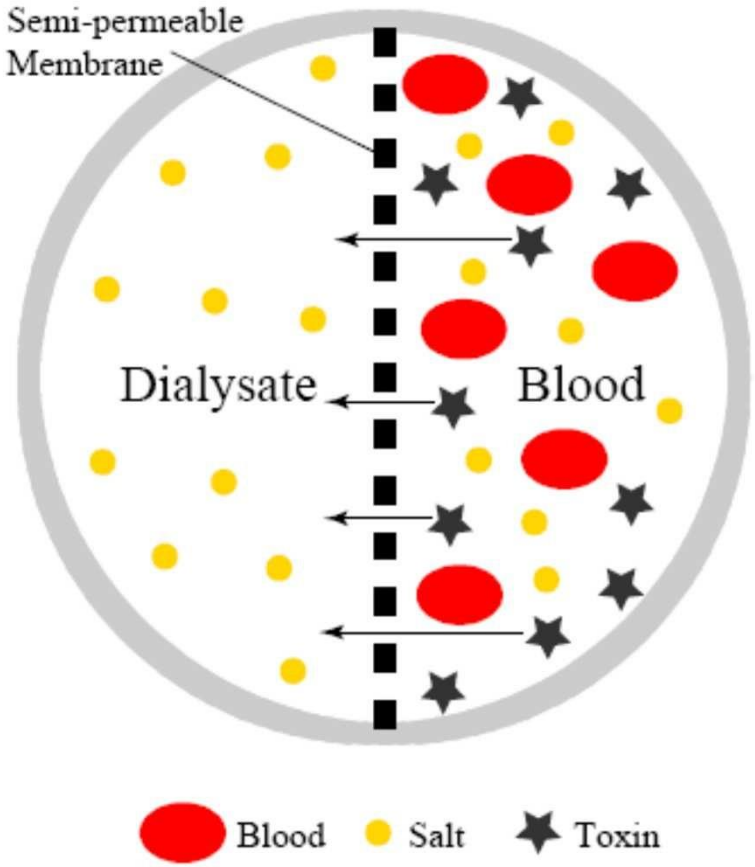
PD MODALITY IN PATIENTS WITH CHF

- The choice of technique depends on renal function (PUF or PD)

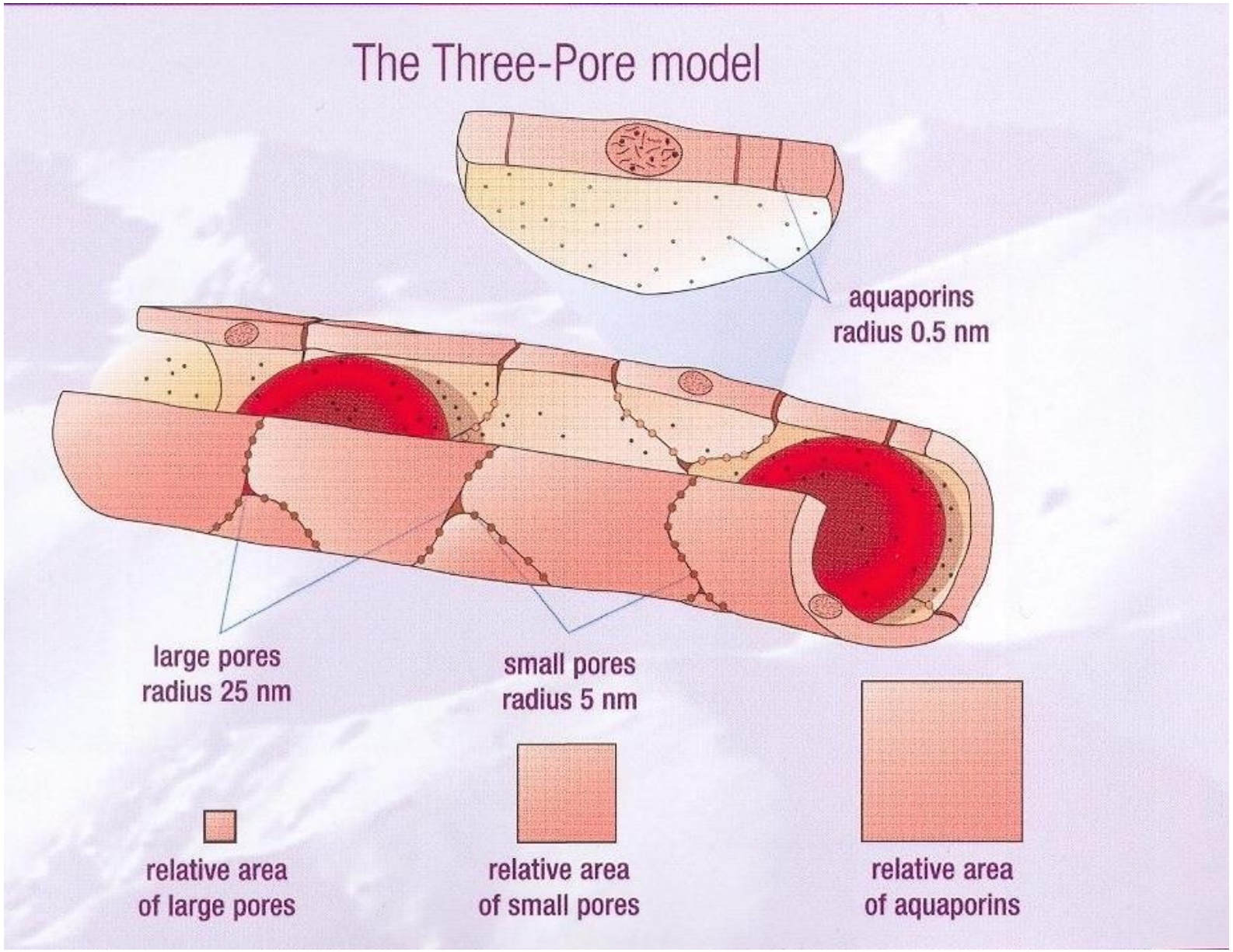
- Patients with coexisting renal failure may be treated with
  - continuous ambulatory PD (CAPD)
  - automated PD (APD)

- Those without significant impairment of renal function
  - a single nightly exchange (PUF) with osmotic agent (optimally, *icodextrin*) is sufficient

PERITONEAL MEMBRANE: SEMI-PERMEABLE

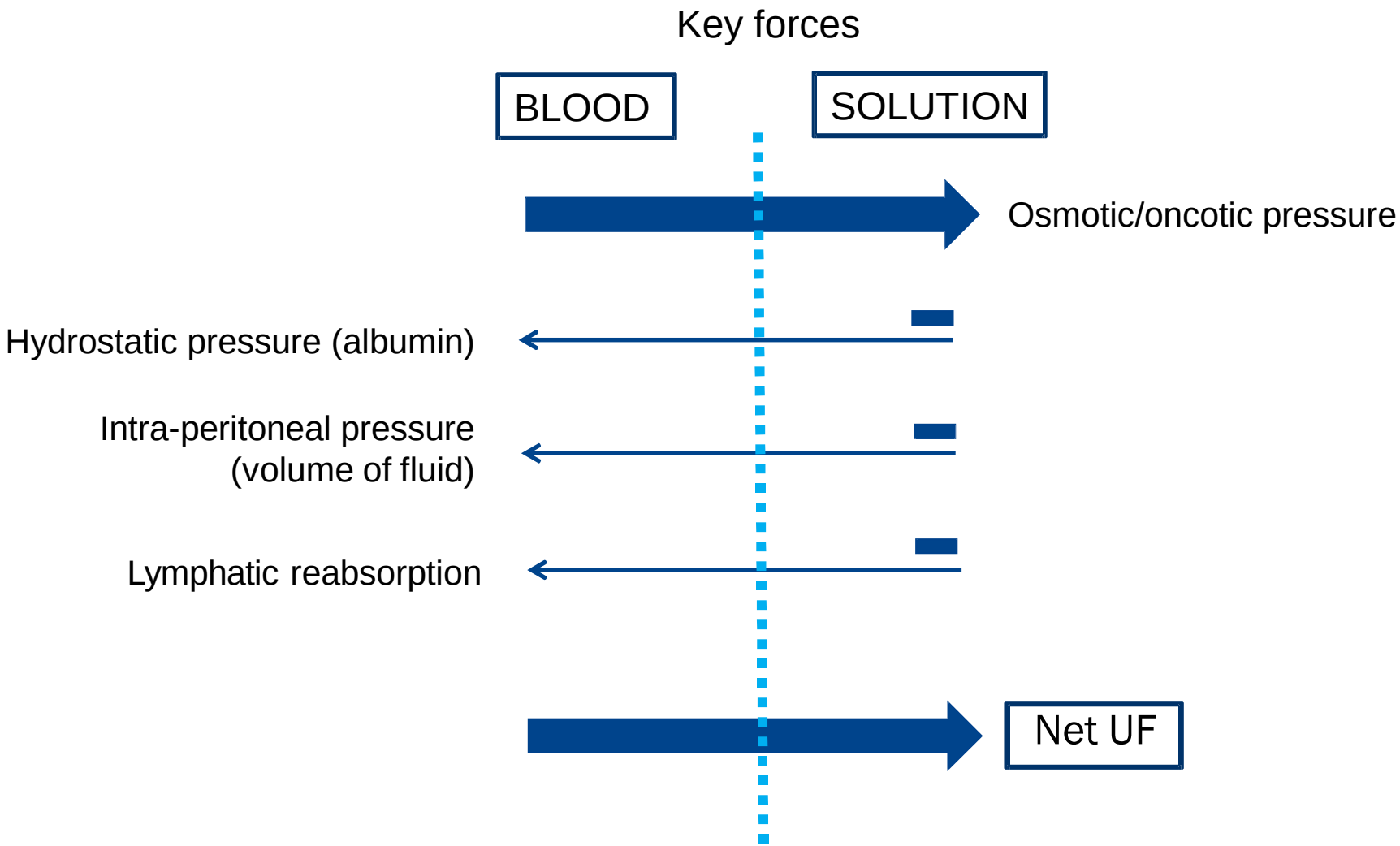


- Designed to keep blood components like red blood cells, platelets and large proteins on the blood side – They cannot pass through the membrane
- The membrane has pores, or openings, that are large enough to allow small molecules to pass, and others not as they are too big
- Also allows water molecules to pass through

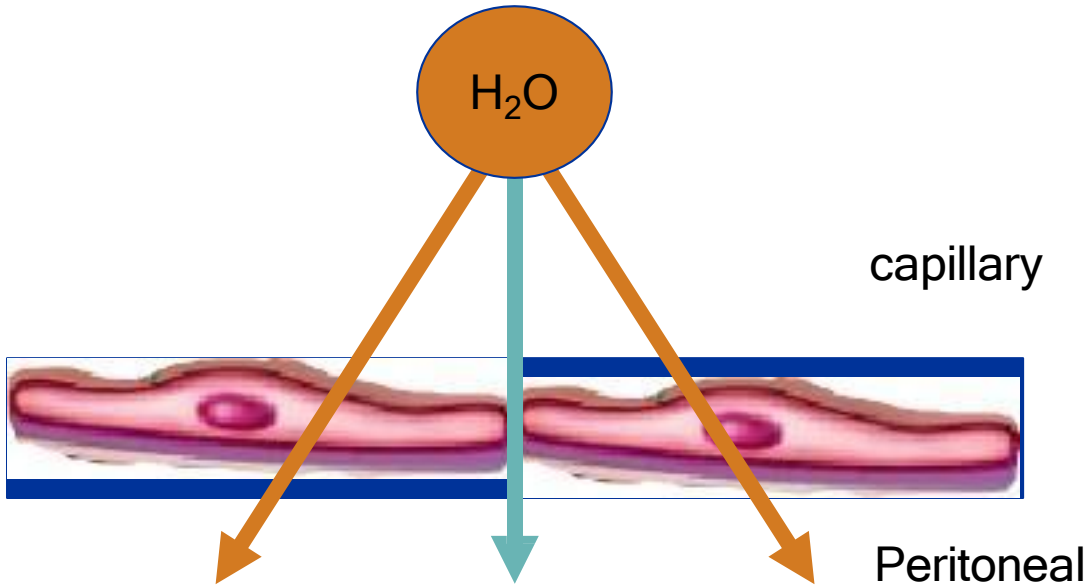


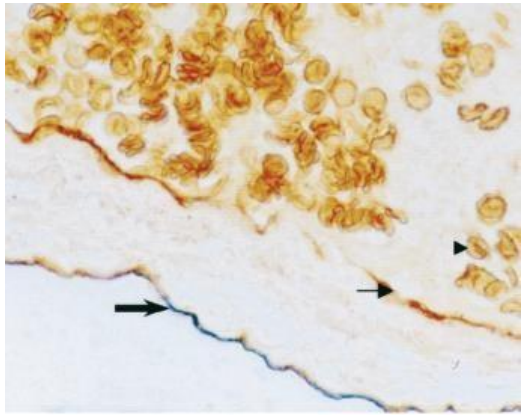
THE THREE - PORE MODEL

FLUID REMOVAL – NET ULTRAFILTRATION

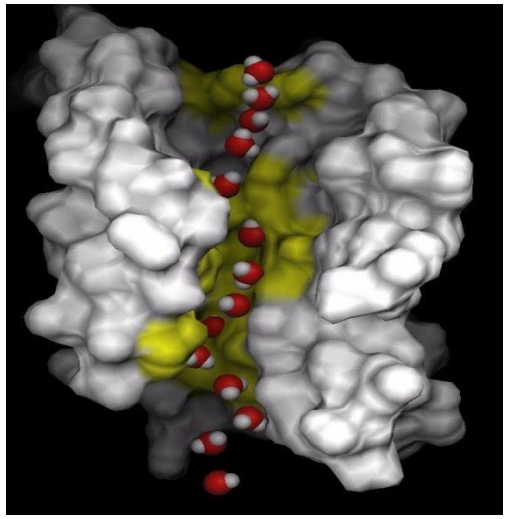


PHYSIOLOGY OF PERITONEAL DIALYSIS: WATER FLOW: ROLE OF AQUAPORINS





Brown=Aquaporin 1

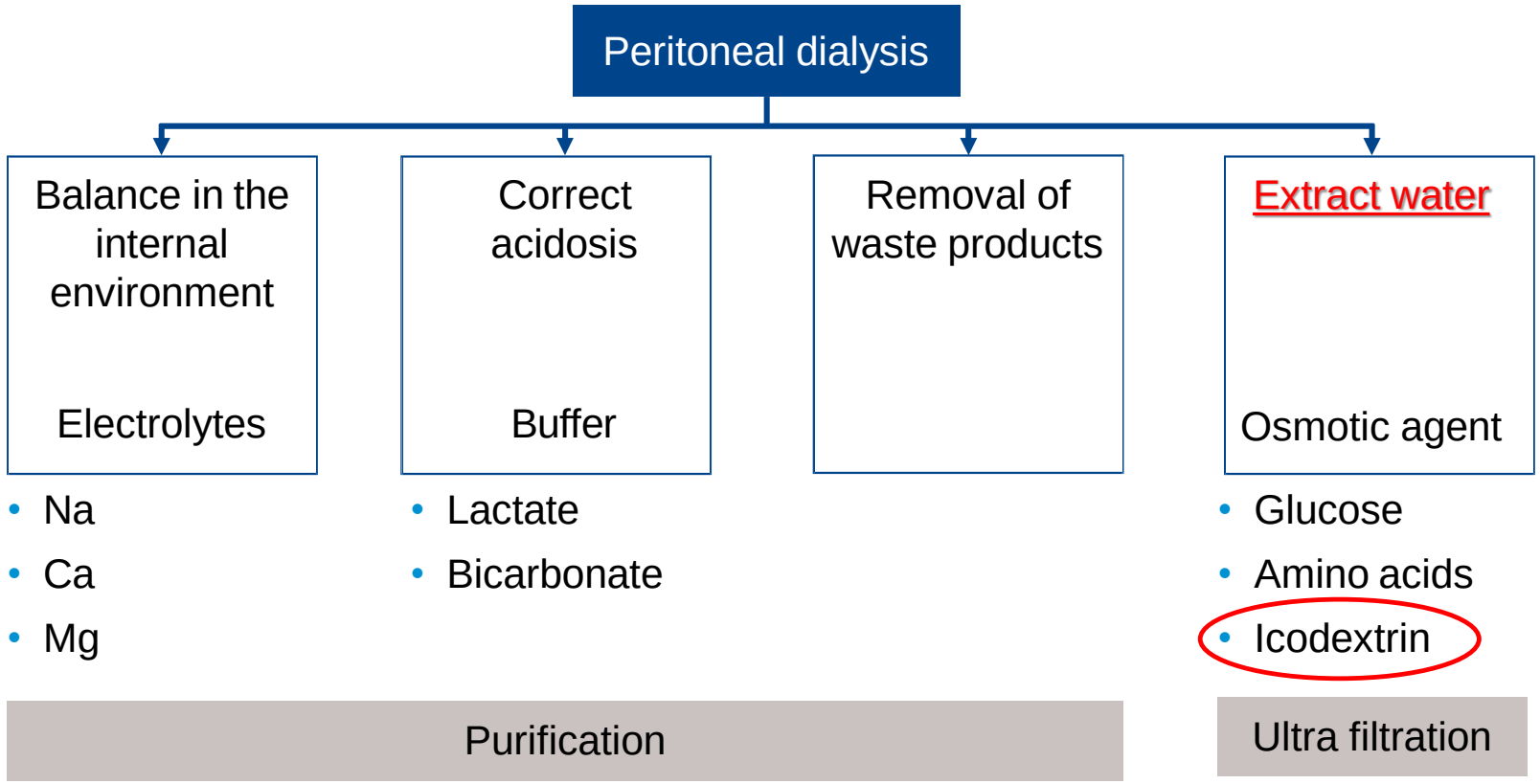


Pathways of water flow:

- 50% aquaporin mediated
- 50% intercellular pathways

Lai et al: J Am Soc Nephrol 2001:12;1036-1045

ROLE OF PD SOLUTIONS



EXTRANEAL SOLUTION

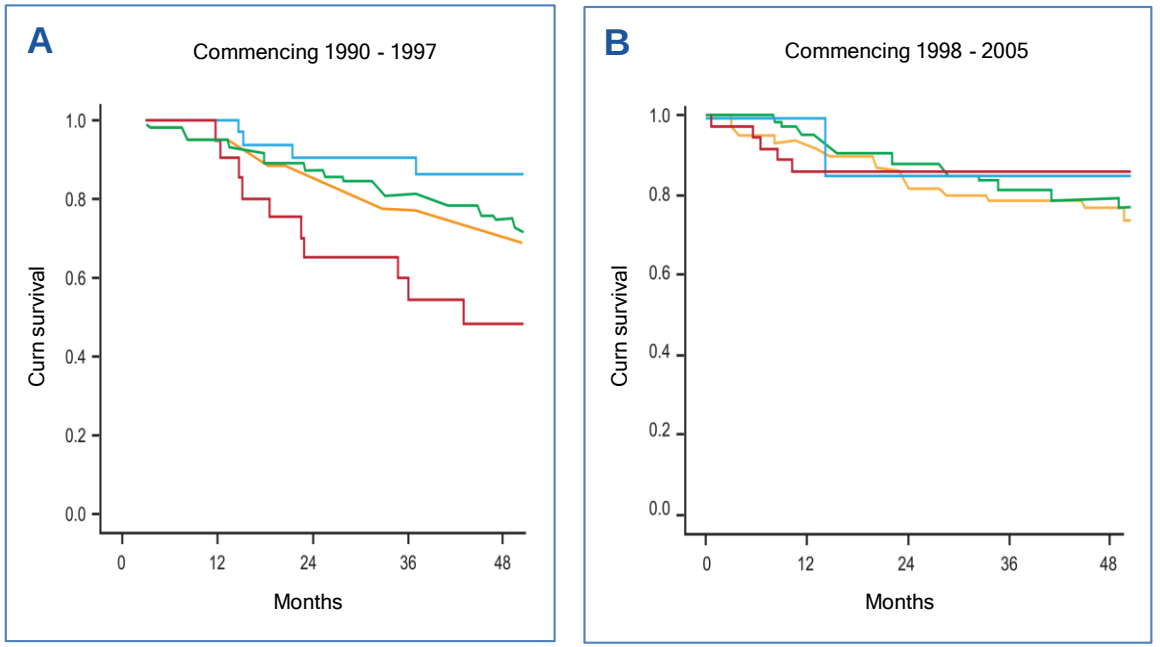
LOGICAL PD PRESCRIBING - CONSIDERING ALL PD THERAPY

The result of focusing on all parameters for all patients.

Patient survival on PD

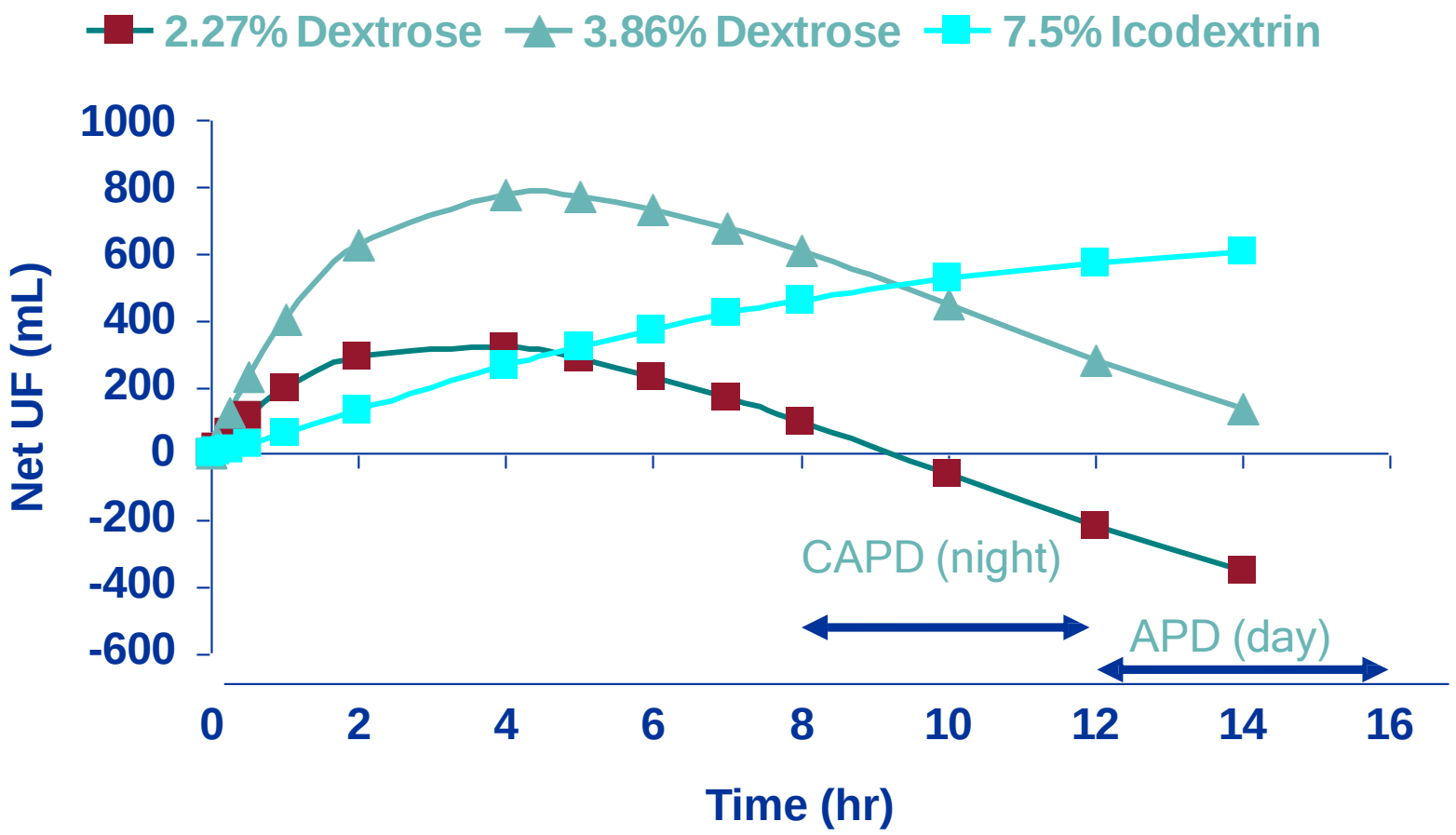
Before the introduction of APD and Icodextrin

After the introduction of APD and Icodextrin



Davis, 2006. Survival on PD according to transport category at the start of treatment in two cohorts commencing between (a) 1990-1997, n=320 and (b) 1998-2005, n = 300. Low (-), Low average (-) High average (-) and High (-). In the first cohort, transport category was significantly (P=0.009) associated with survival, whereas in the second this was not the case due to an improvement in the survival of high transport patients.

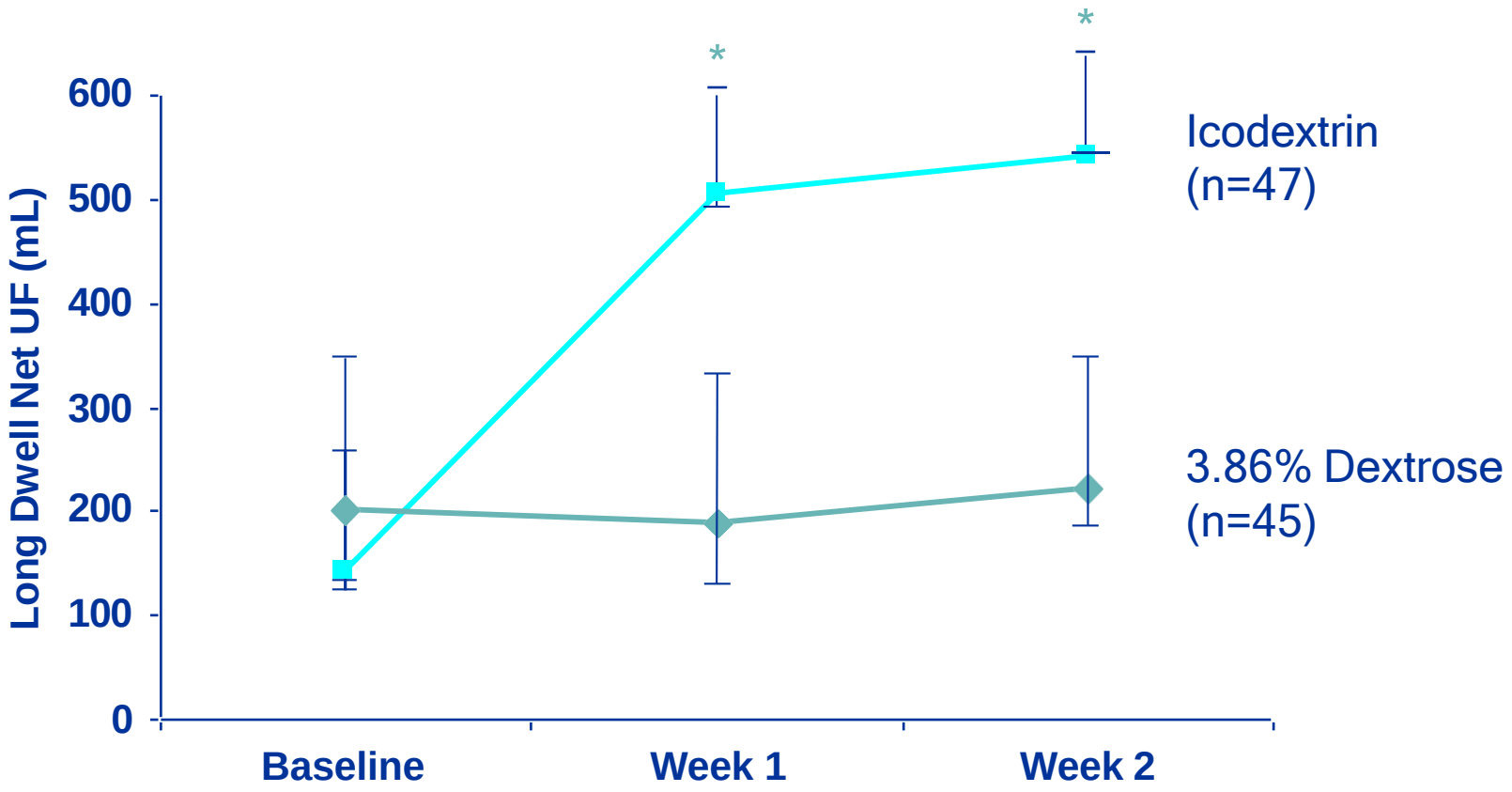
COMPARISON OF NET UF DURING A PD DWELL – SUSTAINED UF FOR THE LONG DWELL



Mujais S, Vonesh E. *Kidney Int* 2002;62(suppl 81):S17-S22

KBCRI

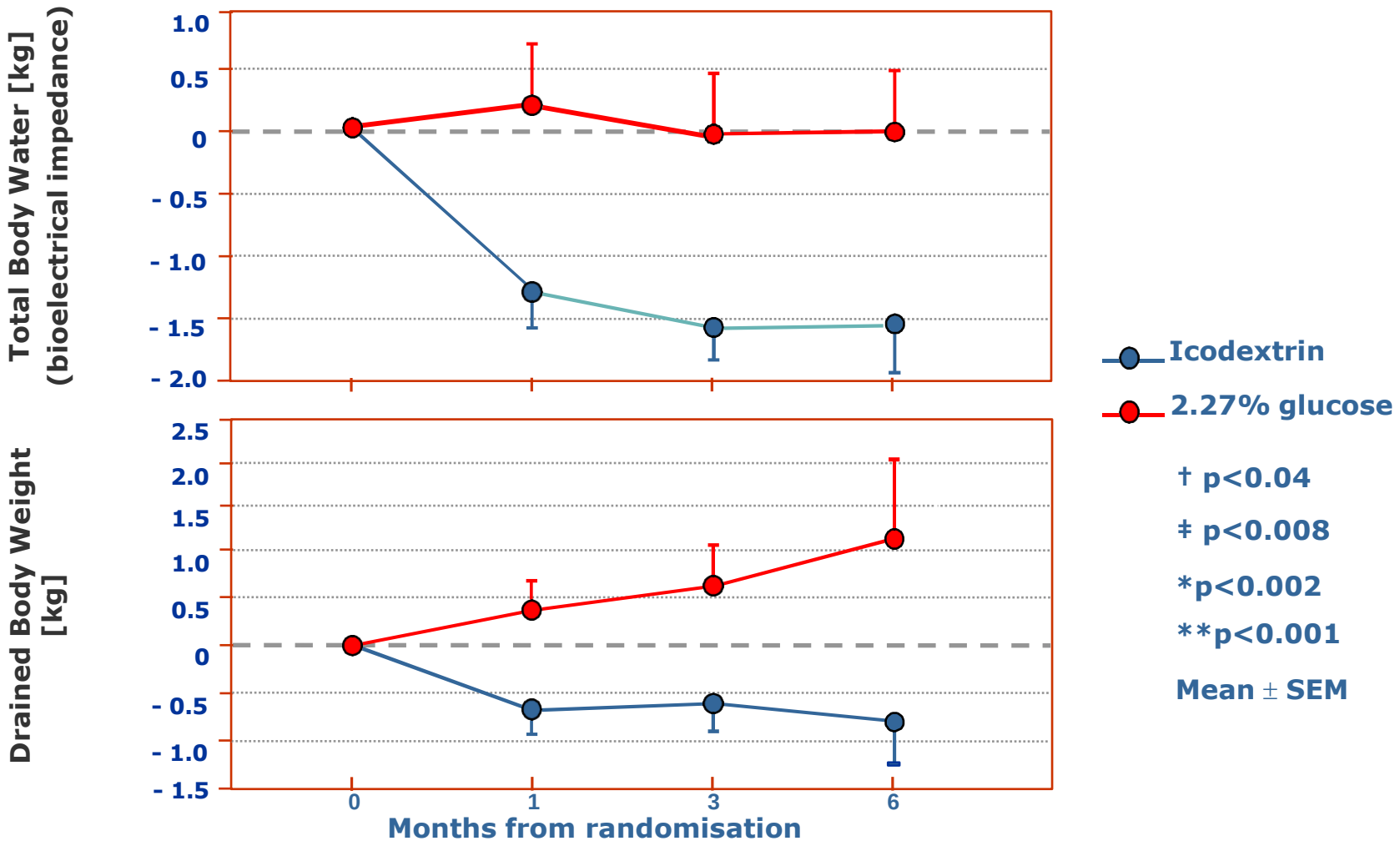
7.5% ICODEXTRIN VS 3.86% DEXTROSE FOR APD LONG DWELL: HIGH TRANSPORT TRIAL



*$P < 0.001$ vs 3.86% dextrose (adjusted for baseline values).

Finkelstein F et al. *J Am Soc Nephrol* 2005;16:546-554

BENEFITS IN REDUCING WEIGHT AND TOTAL BODY WATER WITH 7.5% ICODEXTRIN



Davies SJ et al, J Am Soc Nephrol 14: 2338-2344, 2003

ICODEXTRIN - ADVANTAGES

- Icodextrin solution may be associated with improved patient survival.

  Han SH, *et al. Nephrol Dial Transplant* 2012; 27:2044–2050.

- The use of icodextrin solution has been associated with a lower risk of new-onset CHF in new PD patients vs. those not using icodextrin solution.

  Wang IK, *et al. Pharmacoepidemiol Drug Saf* 2018; 27:447–452.

- Icodextrin solution may be associated with improved profiles of some lipids in some PD patient populations.

  Huang YF, *et al. Biomed Res Int* 2015; 2015:208980.

- Use of icodextrin solution helps maintain peritoneal membrane function and facilitates the achievement of fluid balance.

  Paniagua R, *et al. Perit Dial Int.* 2009; 29:422–432.

- Avoidance of excess glucose exposure can preserve peritoneal ultrafiltration and solute clearance.

  Davies SJ, *et al. Kidney Int* 2005; 67:1609–1615.

PD in advanced CHF (1)

Journal of Cardiology (2010) **55**, 49–54

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/jjcc

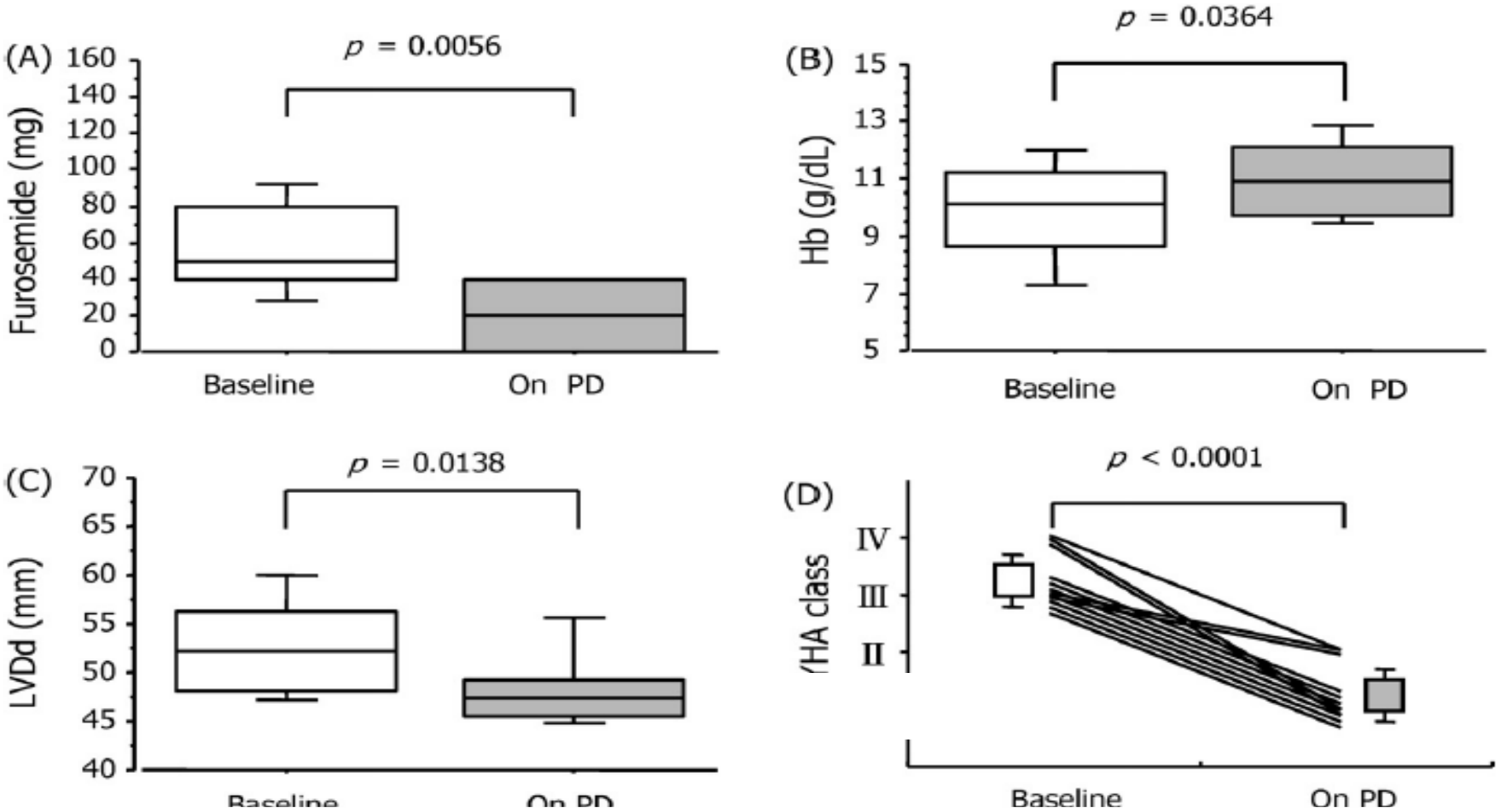
ORIGINAL ARTICLE

Novel therapeutic option for refractory heart failure in elderly patients with chronic kidney disease by incremental peritoneal dialysis

Masaru Nakayama (MD)[a,*], Hirofumi Nakano (MD)[b], Masaaki Nakayama (MD)[c]

Nakayama M, et al. J Cardiol. 2010; 55: 49-54..

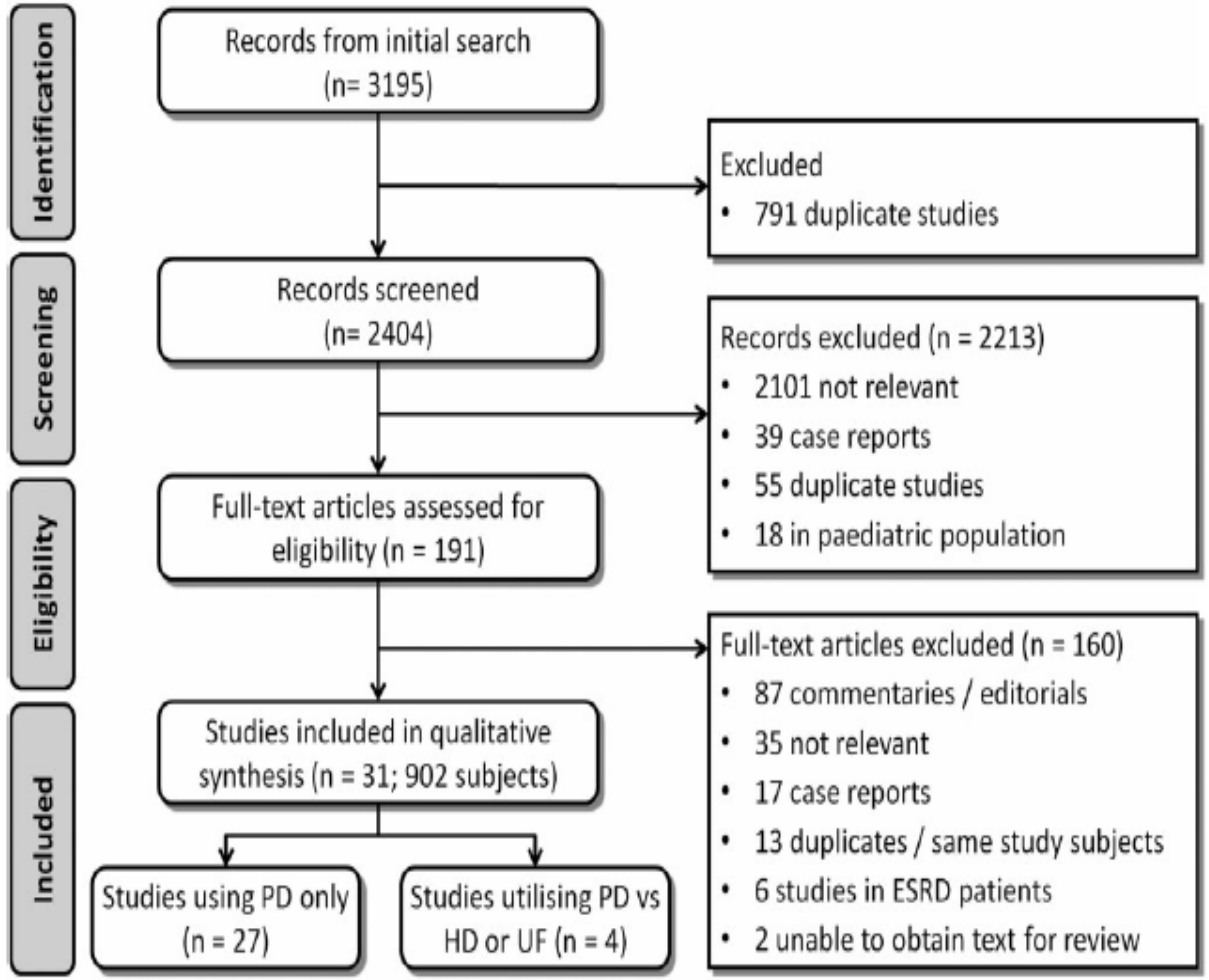
PD in advanced CHF (2)



Nakayama M, et al. J Cardiol. 2010; 55: 49-54..

PD in advanced CHF (3)

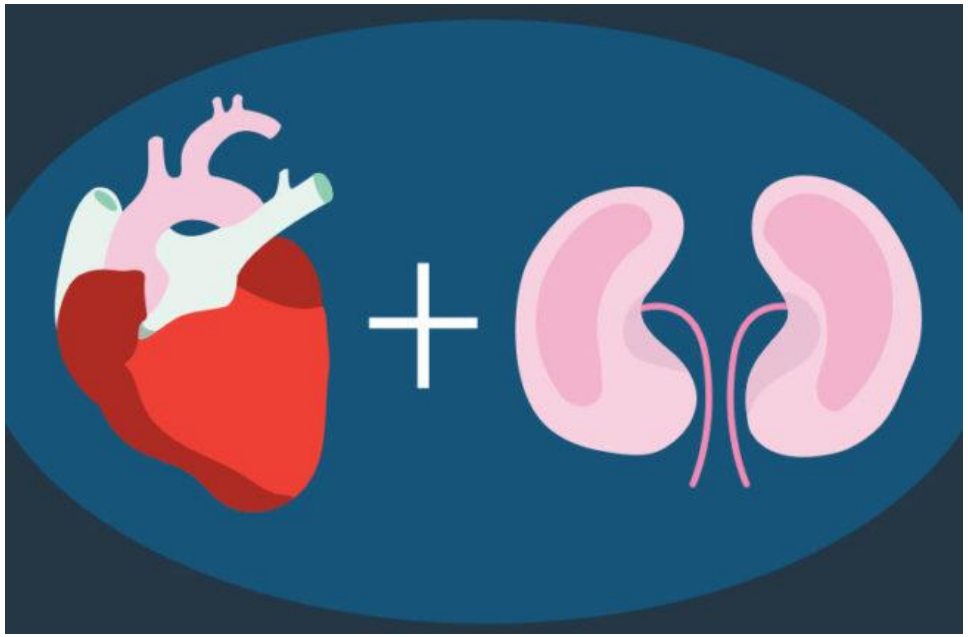
- meta-analysis of 31 non-randomized studies, 1966 – 2017.
- patients treated with PD had fewer symptoms, a lower rate of rehospitalization and a shorter duration of hospitalization compared to patients treated with diuretics
- the comparison of PD with other forms of renal replacement therapy requires additional analyses



Chionh CY. et al. Perit Dial Inter. 2020; 40: 527-39.

PD in advanced CHF (4)

- ultrafiltration therapies, and especially PD, represent potentially useful forms of treatment for patients with **severe CHF, resistant symptoms and frequent hospitalizations**
- an **interdisciplinary approach** with the cooperation of nephrologists and cardiologists seems to be crucial for the successful application of PD in CHF



Puttagunta H, Holt SG. Perit Dial Inter. 2015; 35: 645-9..

CLINICAL HOSPITAL CENTRE RIJEKA – EXPERIENCE

"THE THREE MUSKETEERS"

MULTIDISCIPLINARY TEAM

- Cardiologist – indication, follow - up
- Nephrologist – education, ultrafiltration prescription, follow - up
- Urologist – peritoneal catether placement
- Anesthesiologist – ultrasound-guided transversus abdominis plane (TAP) block anesthesia
- PD nurse – education, follow - up

♂ I.O. 71 YRS OLD, NYHA CLASS IV

Diabetic, insulin treated

2006 myocardial infarction + PCI LAD

2009 PCI LAD, LCx and RCA

9/2011 partial right nephrectomy due to renal cell carcinoma + Double J

12/2017 urosepsis + cardiac arrest with successful resuscitation

01/2018 PCI LAD

05/2018 PCI LAD and RCA

MEDRI

KBCrl

CASE 1 ♂ I.O. 71 YRS OLD, NYHA CLASS IV

- 12/2018 congestive heart failure (CHF, HFmrEF), anasarca, dyspnea
- 12/2018 CHF – anasarca, dyspnea, refractory to diuretics - continuous veno-venous hemodialysis (CVVHD)
- 01/2019 CHV – anasarca, dyspnea, refractory to diuretics - CVVHD
- 03/2019 CHF - anasarca, dyspnea
- 09/2019 CHF - anasarca, dyspnea
- 10/2019 CHF - anasarca, dyspnea
- 12/2019 CHF - anasarca, dyspnea
- 01/2020 CHF - anasarca, dyspnea

Class I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation or dyspnoea.
Class II	Slight limitation of physical activity. Comfortable at rest but ordinary physical activity results in fatigue, palpitation or dyspnoea.
Class III	Marked limitation of physical activity. Comfortable at rest but less than ordinary activity results in fatigue, palpitation or dyspnoea.
Class IV	Unable to carry out any physical activity without discomfort. Symptoms at rest. If any physical activity is undertaken, discomfort is increased.

NYHA: New York Heart Association.

CASE 1 ♂ I.O. 71 YRS. OLD, NYHA CLASS IV

- 02/2020. CHF – refractory to diuretics – slow contious ultrafiltration (SCUF), body weight **100 kg**
- 17.02.2020. peritoneal catether insertion (TAP block anesthesia)
- Intermittent ultrafiltration 3 times per week duration 3 hrs, body weight 81 kg (- 19 kg)
- 08.03.2020. peritoneal catether surgical reposition due to malposition
- 23.03.2020. CAPD education
- 25.03.2020. The patient has fully mastered the skill to independently perform peritoneal dialysis procedures (2 days), start with icodextrin 2000 ml intraperitonelly (IP), 12 hrs night dwell
- 14.04.2020. central venous catether ex, body weight 77,5 kg (- 22,5 kg)
- 10/2020. peritonitis (E.coli) –outpatient treatment, recovered

CASE 1 ♂ I.O. 71 YRS OLD, NYHA CLASS II

date	02/2020.	04/2020	05/2020	06/2020	10/2020	06/2021	07/2021	08/2021	09/2021
NTproBNP (ng/L)	24017	11214	16396	8452	10821	14402	17455	19937	19045
Albumin (g/l)	35,5	37,7	36,9	38,9	42,2	40,1	38,1	38,4	40,6
eGFR CKD-EPI ($ml/min/m^2$)	18	23	24	17	18	16	17	17	16
24 hrs diuresis (ml)	2500	1650	1700	1500	2000	2000	2000	2500	1500
24 hrs ultrafiltration (ml)	0	500	700	700	600	650	600	550	800
body weight (kg)	100	78,4	79	78,5	83	81,5	82	83	81,5

NYHA class IV → NYHA class II

CASE 1 ♂ I.O. 71 YRS OLD, NYHA CLASS II

15.9.2021. cardiology examination: The patient feels good. ***Since being treated with peritoneal ultrafiltration there are no symptoms of heart failure.***

Clinical status: BP 155/90 mmHg.
The action of the heart is arrhythmic, the tones are clear, no heart murmurs, auscultatory bilateral ***normal respiratory murmur***.

No edema present.

THANK YOU