Management of a patient with Ultrafiltration failure

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Special Series/Guidelines

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SAGE

ISPD recommendations for the evaluation of peritoneal membrane dysfunction in adults: Classification, measurement, interpretation and rationale for intervention

Johann Morelle[1], Joanna Stachowska-Pietka[2], Carl Öberg[3], Liliana Gadola[4], Vincenzo La Milia[5], Zanzhe Yu[6], Mark Lambie[7], Rajnish Mehrotra[8], Javier de Arteaga[9] and Simon Davies[7]

Disclosure

- Speaker and consultant for Outset Medical Inc.

Case base discussion to understand :

- Approach to initial management of fluid overload in a PD patient
- The clinical significance of ultrafiltration & volume management in a Peritoneal dialysis patient ?
- Identification of Ultrafiltration insufficiency (PD membrane dysfunction) phenotypes - per ISPD guidance
- Management of Ultrafiltration insufficiency - per ISPD guidance

A 60 -year-old female with ADPKD & DM2 who started APD, 3 months ago presents with peripheral edema and SOB.

- Her BP was 170/90 mm Hg and she gained 4 kg from her last monthly clinic visit.
- JVP distended, peripheral edema, normal cardiac and respiratory examinations were noted.
- Her APD was prescription of four 2-L overnight exchanges of 1.5 % (over 8 hours)
- Her reported urine output was = 700 ml/d (with kt/v)
- Daily Ultrafiltration(UF) = 500 ml/d (with kt/v)
- 2 D Echo : Normal EF , Diastolic dysfunction

What are the consequences of fluid overload for this PD patient ?

- Patient reported out come : SOB , edema
- Hospitalization
- Poor cardiovascular outcomes : hypertension , LVH
- Technique failure
- Mortality

Vrtovsnik et al. CKJ 2021. (IPOD-PD study)
Van Biesen et al. CJASN 2019
Flythe et al. ASN 2021 Abstract.
Ng et al. PLoS One 13: e0202203, 2018

Approach to evaluation of this PD patient with fluid overload

INPUT/INTAKE

OUTPUT

Increase in salt and fluid intake

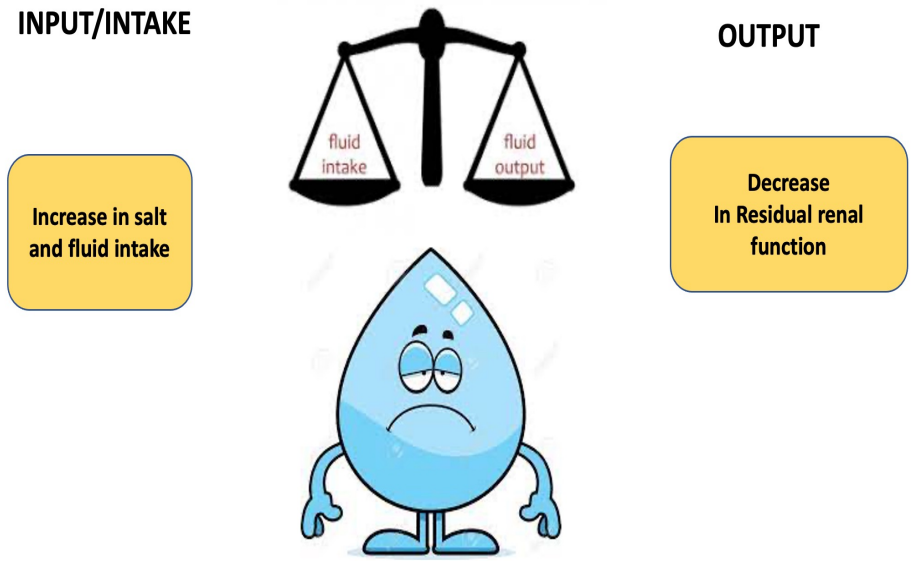
Decrease In Residual renal function

Decrease in UF with normal PD membrane function
OR
Decrease in UF with PD membrane dysfunction

Fluid overload in a PD patient : Adequate PD Ultrafiltration (or underlying inadequate UF)

POTENTIAL REASONS

- Non-adherence with salt and fluid restrictions
- Drop in residual renal function
- New onset heart or liver disease



INTERVENTIONS

- **Salt restriction**
- **Fluid restriction**
- **U/O and weight diary**
- **Diuretic (choice and dose of diuretics)**
- **Strategies to preserve RRF**
- **Adjust PD prescription/PD fluid concentration**
- **Remote patient monitoring and close follow-up of RPM data and patient symptoms**

Fluid overload in a PD patient -Inadequate PD Ultrafiltration (with normal PD membrane function)

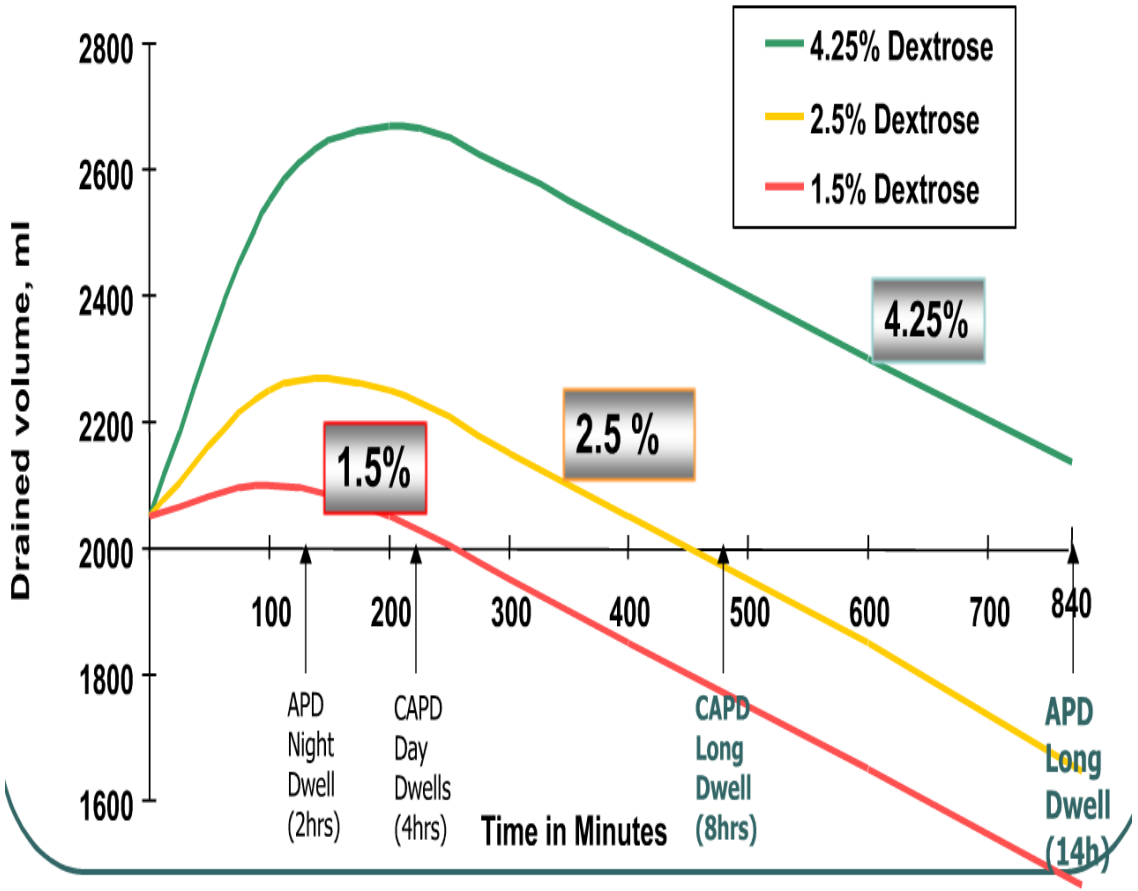
POTENTIAL REASONS

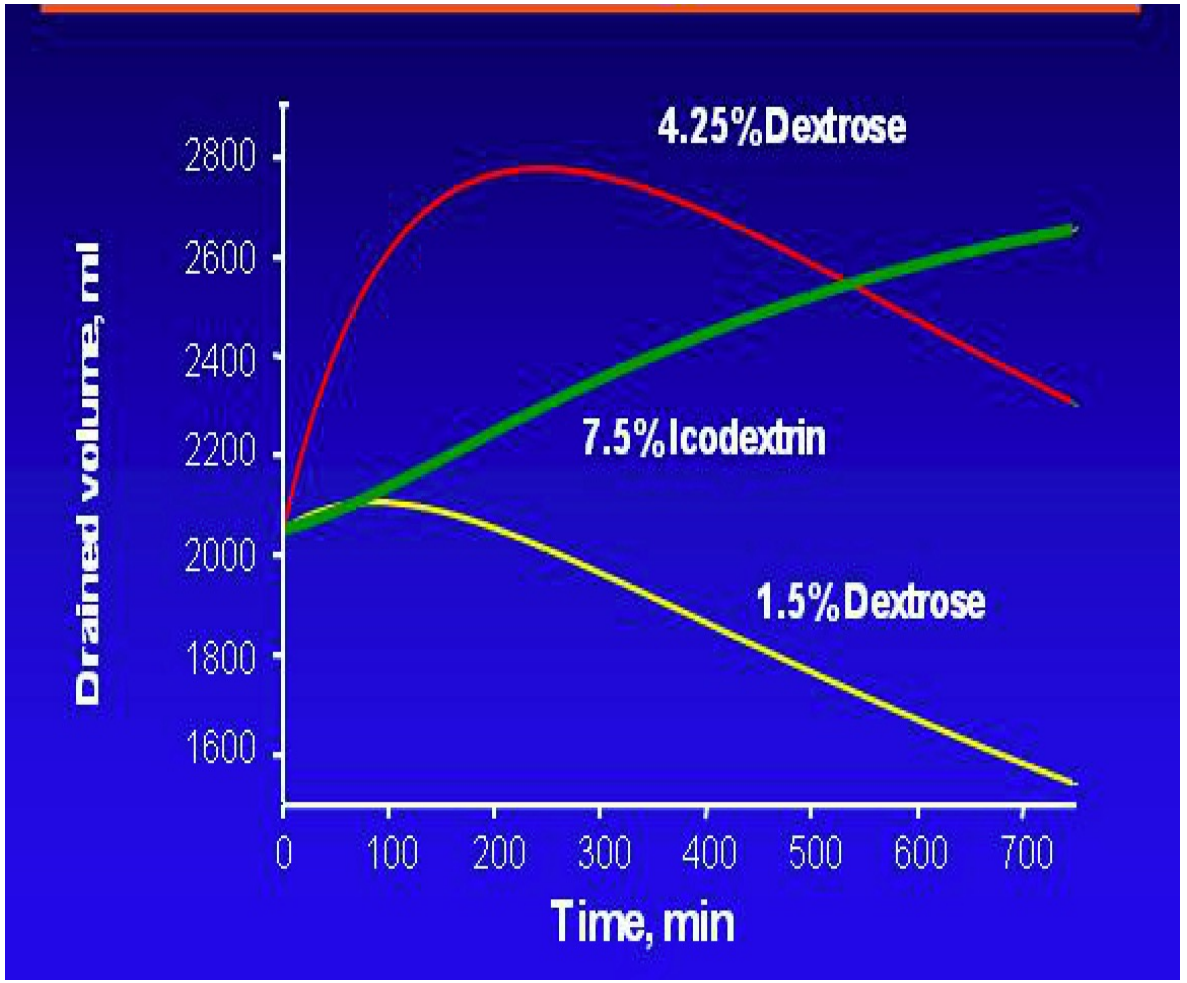
- Non-adherence to PD prescription
- Poor knowledge regarding choice of PD bags and trouble-shooting
- PD catheter dysfunction
- Sequestration of PD fluid-PD fluid leaks

INTERVENTIONS

- **Re-educate patient**
- **High risk approach/close follow-up**
- **Analyze the RPM data**
- **Trouble shoot PD catheter dysfunction**
- **Management of leaks**

Ultrafiltration profile Dextrose vs Icodextrin





Rippe et al . KI . 2000

Management of acute fluid overload

- Short term frequent hypertonic solutions (4.25% dextrose every 3–4 hours) should be prescribed as either manual exchanges or via APD, continuously, at day and/or night
- Icodextrin should not be used in acute symptomatic volume overload because of the slower fluid removal profile relative to dextrose solutions

A 60 -year-old female with ADPKD & DM 2 (started APD 3 months ago) who presented with peripheral edema and SOB.
Daily UF ~ 500 ml and u/0 ~ 700 ml

- Educated to restrict salt and water (patient not happy !!)
- Diuretic – Bumex was started
- Patient was educated to incorporate use of 2.5 % based on symptoms, weight and UF volume
- She was monitored closely with RPM data (weight ,UF volume) and u/o volume
- Euvolemic **(Month 3 clinic visit)**

- Daily u/o as per patient improved (~ 900 ml)
- Daily UF improved ~ 600-800 ml

Month 5 & 6
A 60 -year-old female with ADPKD & DM 2 presents with progressive fluid overload symptoms

- Daily u/o = 200 ml/d on Bumex 4 mg per day (she had coronary angiography for Tx evaluation and UTI at month 4)
- Daily UF with 2.5% and 1.5% = 500-600 ml
- Symptoms and UF improve with use of 4.25 %
- Wants to avoid 2.5 % and 4.25 % due to hyperglycemia

What information is missing so far ?

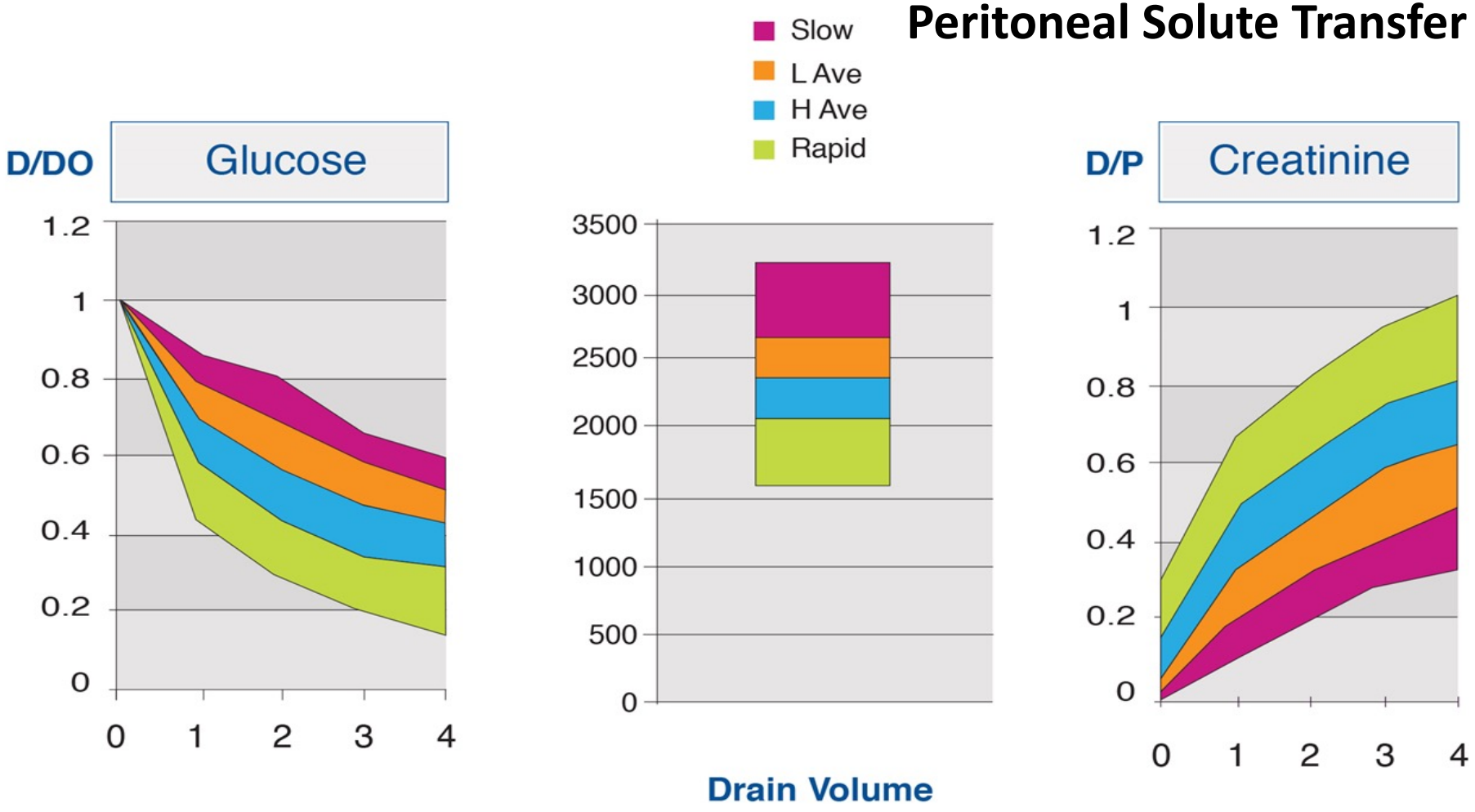
Peritoneal Dialysis International
www.pdiconnect.com

Perit Dial Int **July/September 1987** vol. 7 no. 3 **138-148**

PERITONEAL EQUILIBRATION TEST

Zbylut j. Twardowski, Karl O. Nolph, Ramesh Khanna, Barbara F. Prowant, Leonor P. Ryan, Harold L. Moore and Marc P. Nielsen

Peritoneal Solute Transfer Rate (PSTR)



ISPD recommendations (PET)

- PSTR should be determined from a 4-h PET, using either 2.5% or 4.25% dextrose solution and creatinine as the index solute. (practice point) .
- This should be done early in the course dialysis treatment (between 6 weeks and 12 weeks) (GRADE 1A) and subsequently when clinically indicated.

Morelle et al. PDI 2021

ISPD recommendations : Clinical implication fast PSTR

A faster PSTR is associated with lower survival on PD. (GRADE 1A). This risk is in part due to the lower ultrafiltration (UF) that occurs when the PSTR is above the average value.

Outcomes	Source	Number of patients	Adjusted relative risk (95% CI) per 0.1 increase in D/P creatinine
All-cause mortality	Brimble meta-analysis 2006[103] 19 studies, includes CANUSA study, Stoke Study,[104] EAPOS and ANZDATA Registry.	6648	1.15 (1.07–1.23)
	Global Fluid Study 2013 (10 centres from UK, Korea and Canada)42		
	Incident cohort	499	1.12 (0.98–1.23)
	Prevalent cohort	307	1.18 (1.003–1.41)
	Davita database 2015 (764 US centres)45	10,142	1.07 (1.02–1.13)
Technique Failure	Brimble KS meta-analysis 2006 6 studies	5104	1.18 (0.96–1.46)
(death censored)	Davita database	10,142	1.01 (0.98–1.05)
Hospitalization	Davita database 2015	10,142	1.05 (1.03–1.06)

Morelle et al. PDI 2021

ISPD recommendations : Mitigation of Fast PSTR

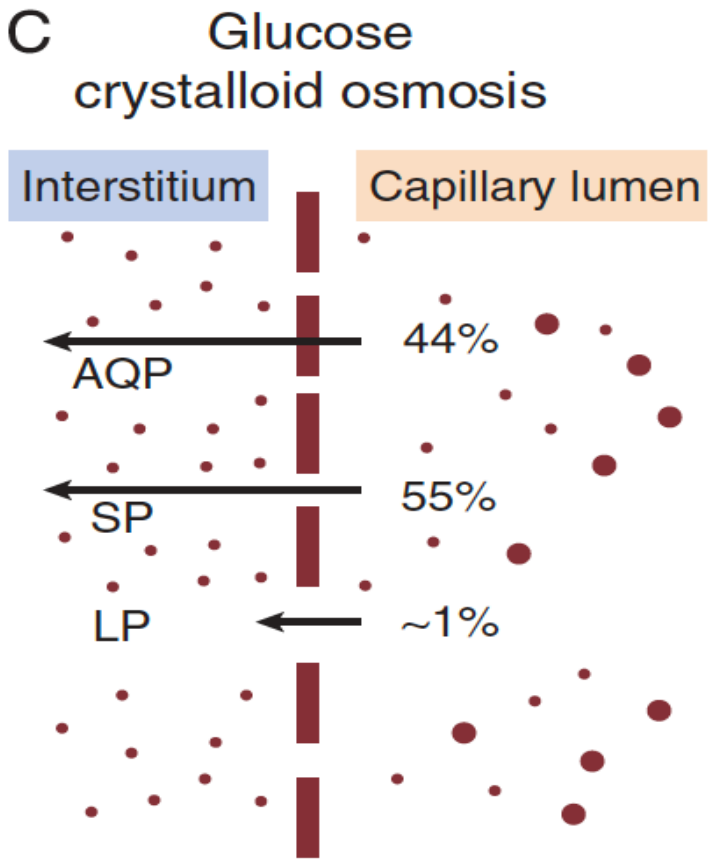
- Lower net UF with fast PSTR can be avoided by (Grade 1 A) :

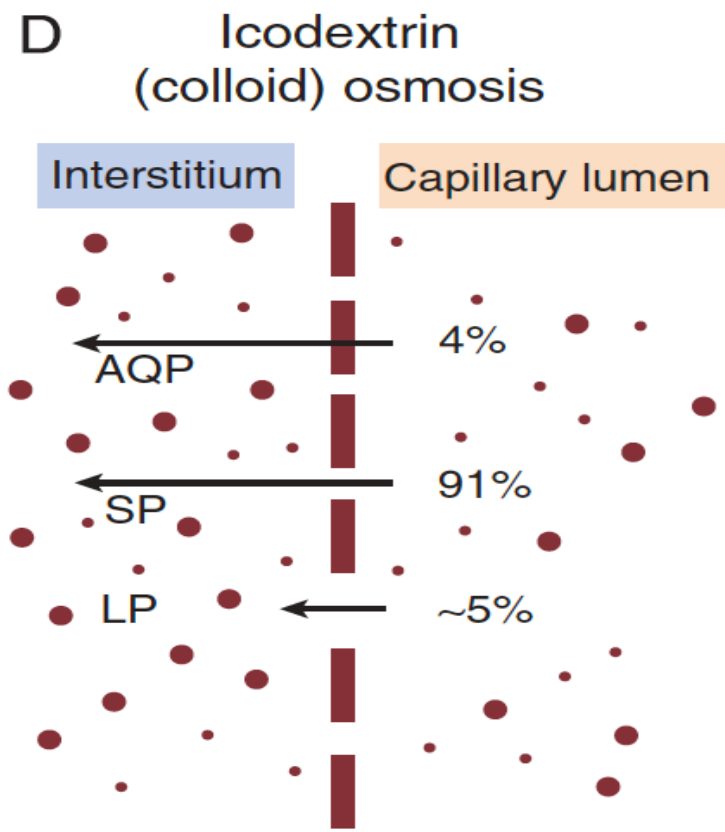
- shortening glucose-based exchanges
- using icodextrin
- and/or prescribing higher glucose concentrations.

- Compared to glucose, use of icodextrin can translate into improved fluid status and fewer episodes of fluid overload. (GRADE 1A)
- Use of automated PD and icodextrin may mitigate the mortality risk associated with fast PSTR. (practice point)

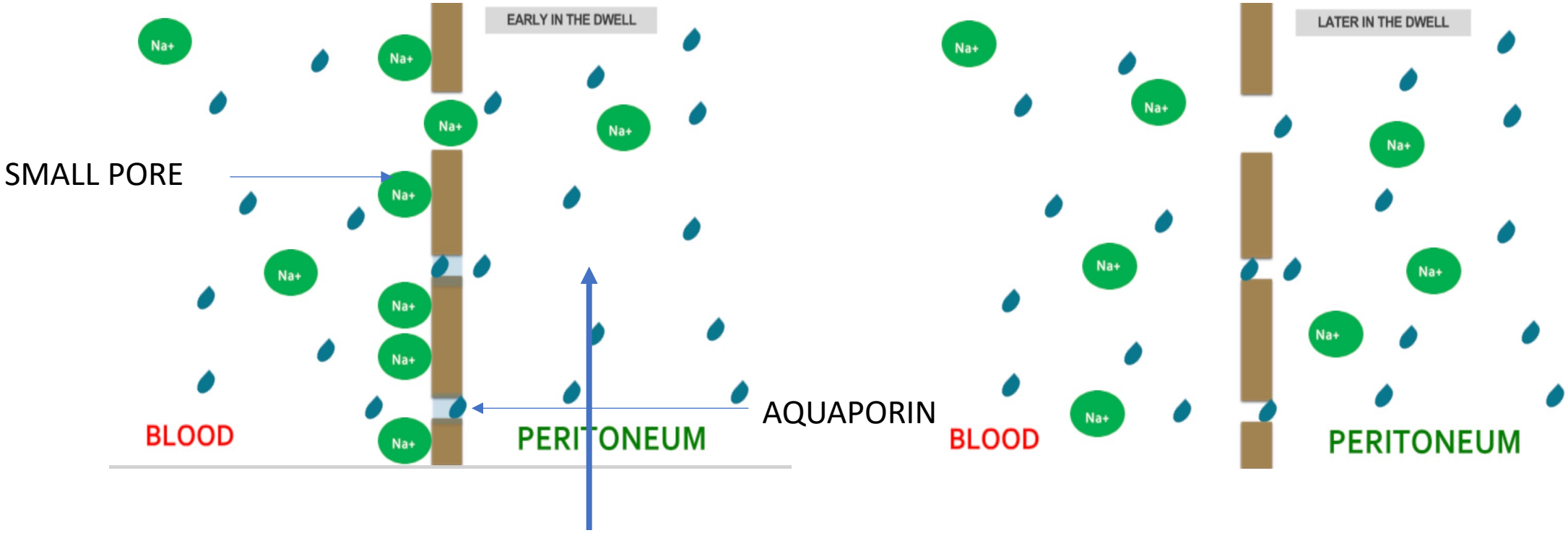
Morelle et al. PDI 2021

Crystalloid vs Colloid osmosis



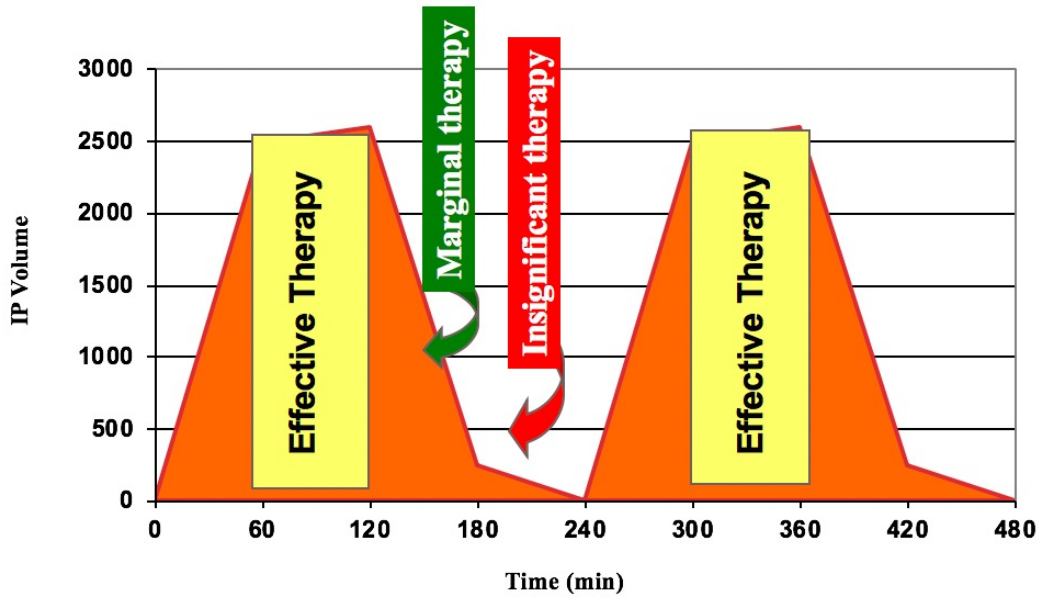


Sodium sieving with Dextrose/crystalloid based solutions



Drop in dialysate Na concertation in PD fluid (DIP) observed during the first hour of a hypertonic glucose dwell (typically about 7–9 mmol/L at 60 min with hypertonic glucose solution).

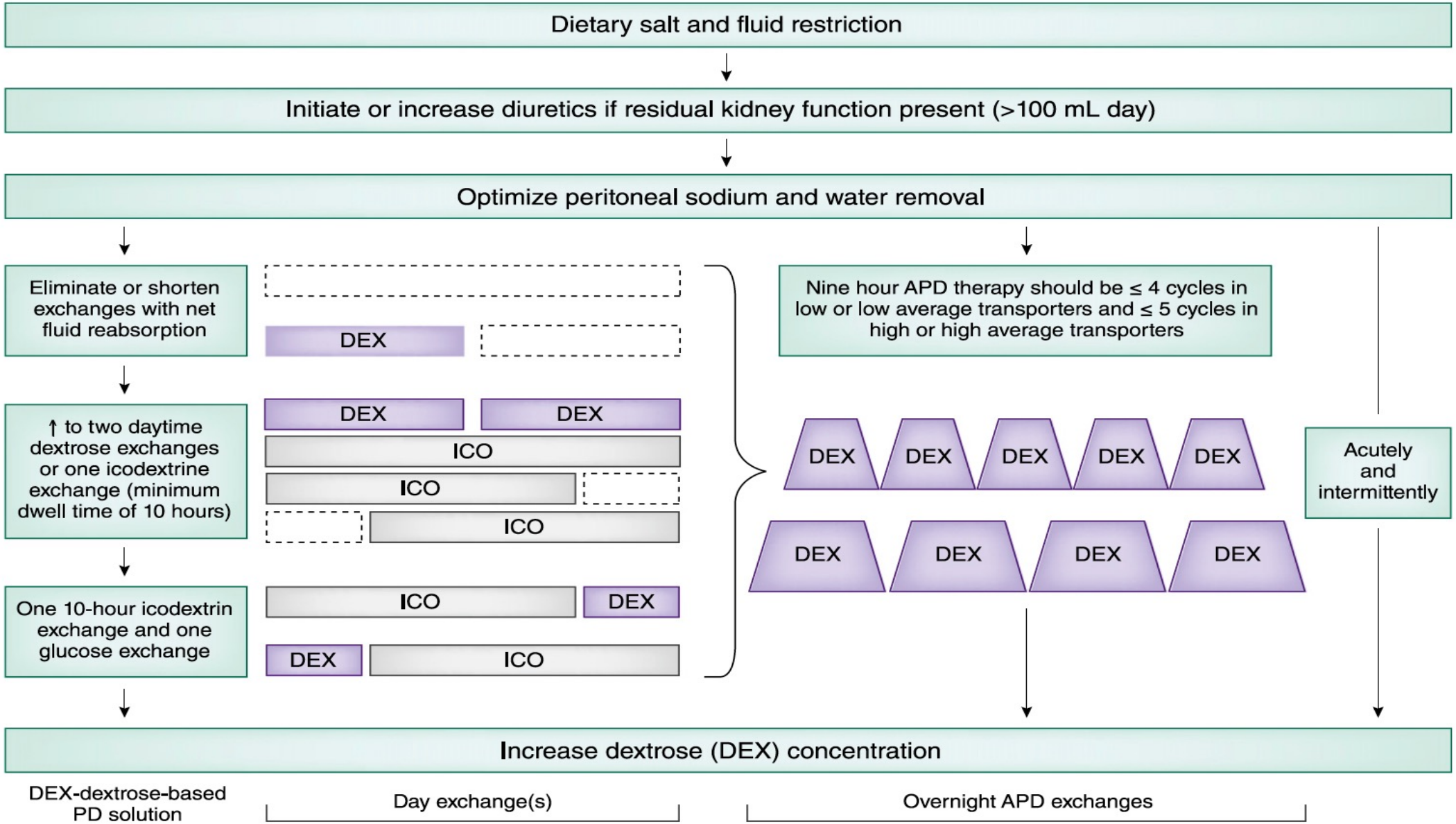
Draw backs of increasing number of exchanges/ rapid cycling



- Less efficient therapy
- Sodium sieving – Na retention, thirst ,fluid overload, HT
- Less middle molecule clearance
- More fluid used – costs

- ALTERNATIVE :

- Use diuretics – with rapid tx
- Icodextrin – with rapid tx



Trinh et al . cJASN 2018

Month 18 : A 60 -year-old female with ADPKD presents with fluid overload symptoms

- Fast PSTR (D/P creatinine =0.74) with PET done at month 3
- **Current PD regimen : 2 L , 4 exchanges over 8 hours & Last fill (2L) with Icodextrin from Month 6 .**
- Daily u/o NIL (gradual decline in u/o)
- Gradual decline in Daily UF from 12 month = NIPD with 2.5 % ~ 200-250 ml & Icodextrin ~ 200-250 ml
- Patient does not want do mid-day exchange i.e enhanced PD

What is going on ? What next ?

Ultrafiltration insufficiency : Low UF capacity due to Membrane dysfunction

Per ISPD recommendation :

Low UF Capacity due to membrane dysfunction is suspected when either :

(a) the net UF from a **4**-h PET is <**4**00 ml (**4**.25% dextrose) or <100 ml (2.5% dextrose), (GRADE 1B)

and/or

(b) the daily UF is insufficient to maintain adequate fluid status. (practice point)

Ultrafiltration insufficiency : Low UF capacity due to Membrane dysfunction

- When insufficient UF is suspected, the 4-h PET should be supplemented by measurement of the sodium dip at 1 h using a 4.25% dextrose exchange
- A sodium dip is expressed as absolute fall in the dialysate Na concentration from baseline $[Na^+]_{t=0} - [Na^+]_{t=60min}$
- A sodium dip of < 5 mmol/L and or a sodium sieving ratio 0.03 at 1 h indicates UF insufficiency. (GRADE 2B)
- Sodium sieving ratio: $1-([Na^+]_{t=60min}/[Na^+]_{t=0}$

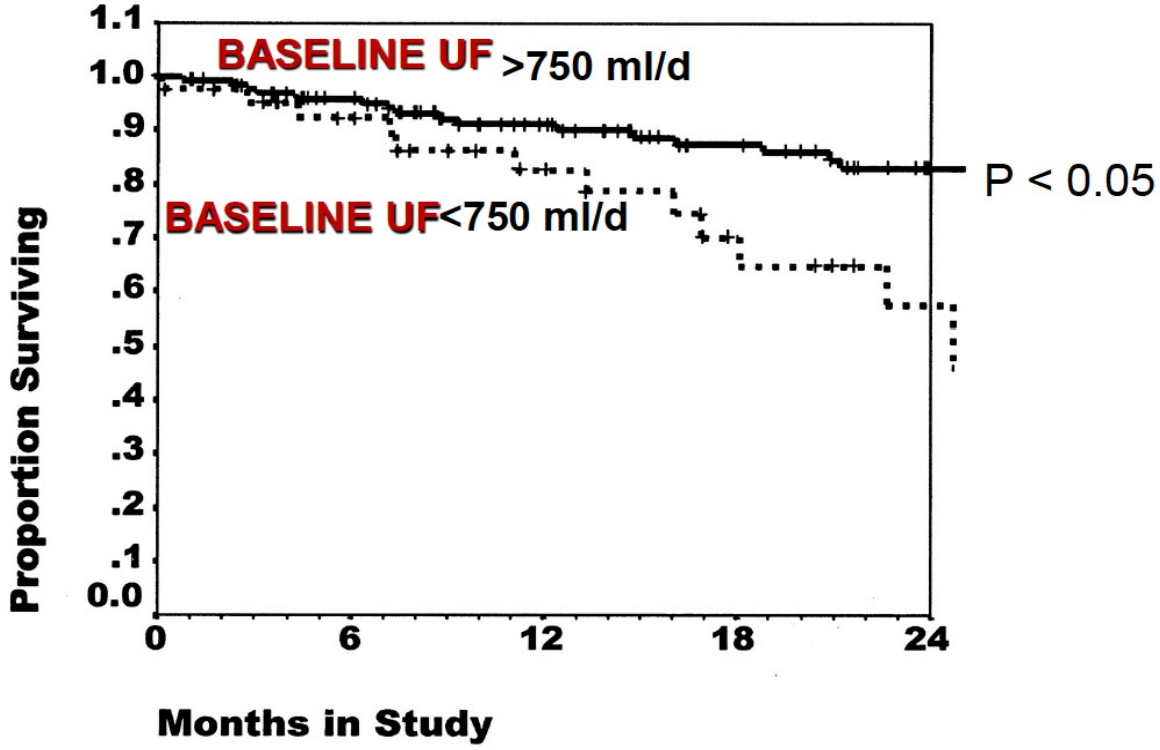
Significance of low Ultrafiltration volume / UF failure / Membrane dysfunction in peritoneal dialysis patients

- Fluid overload symptoms
- Patient reported outcomes (SONG-PD)
- Hospitalizations
- **Technique failure**
- **Mortality**
- Risk of encapsulating peritoneal sclerosis.

Manera K et al. KI 2019

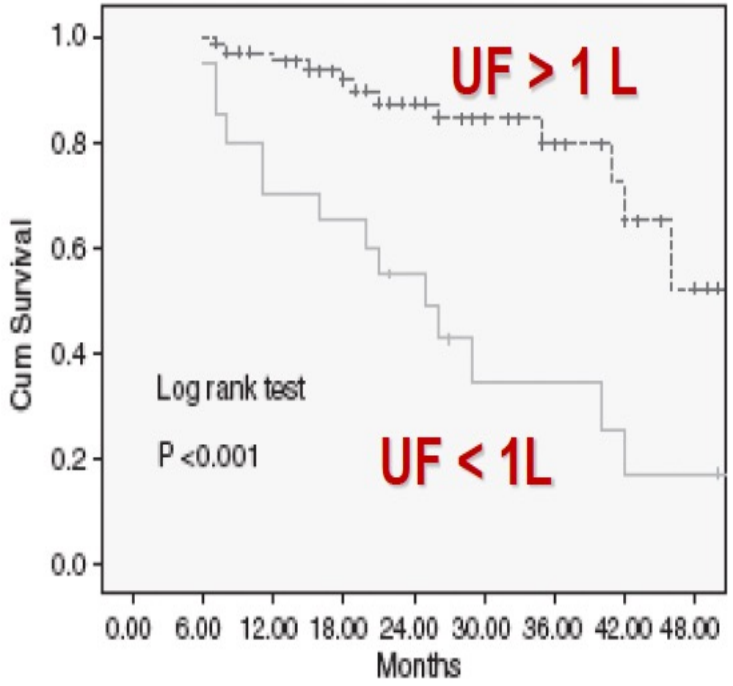
Association between low PD UF and mortality

EAPOS Study



Brown et al. JASN 2003

Anuric PD patients

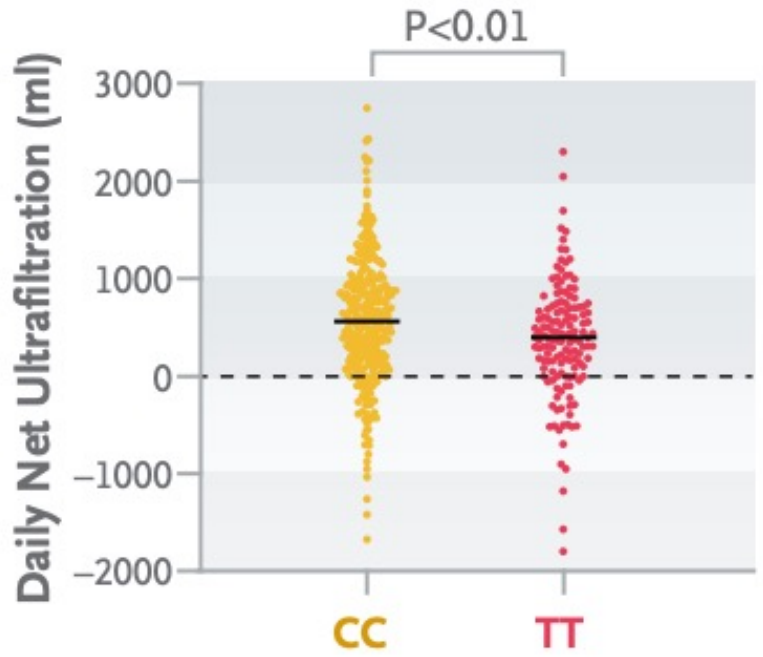


Lin et al. NDT 2010

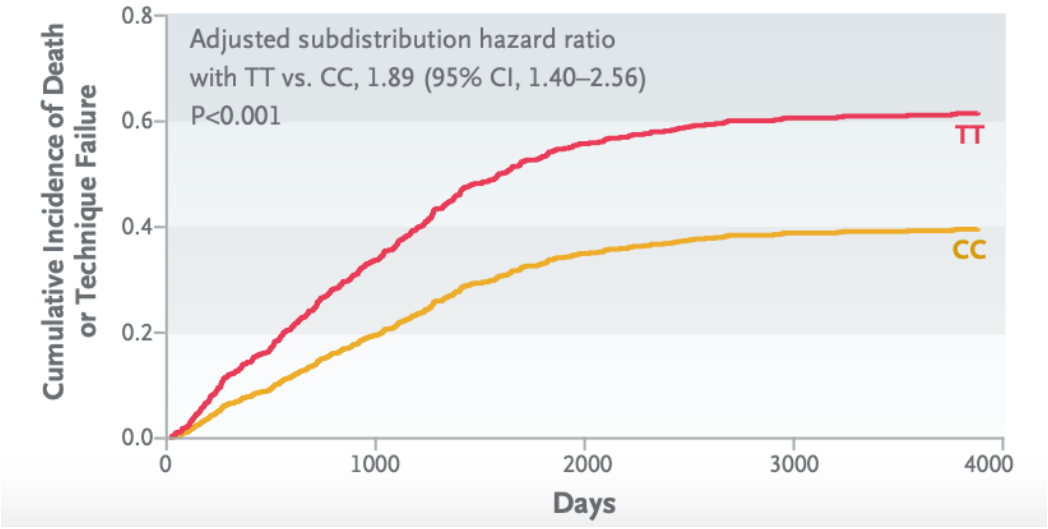
Significance of Optimal Ultrafiltration in peritoneal dialysis patients

In patients undergoing peritoneal dialysis, a common AQP1 variant was associated with decreased ultrafiltration and an increased risk of the composite of death or transfer to hemodialysis.

Daily Net Ultrafiltration according to AQP1 Genotype at rs2075574



Risk of Composite Outcome According to *AQP1* Genotype at rs2075574



Morelle et al .NEJM 2021

ISPD : Classification of membrane dysfunction, including definition, underlying pathophysiology and clinical implications.

Classification	Definition	Pathophysiology	Clinical management
Fast PSTR It can be present at the start of PD and/or develop or resolve over time Morelle et al. PDI 2021	D/P creatinine ratio above 0.65 end of a 4-h PET using either 2.5% or 4.25% dextrose-based Solution	• Membrane inflammation • Neovascularization • Both the above • ? Genetically determined	• With significant RRF, 'dry' nights when treated with CAPD or partial or complete 'dry' days when treated with APD. • Use icodextrin (daytime for APD, overnight for CAPD). • Shorten glucose-based overnight dwells when using APD coupled with icodextrin • If neither APD nor icodextrin available increase glucose strength to prevent reabsorption.

Classification of membrane dysfunction, including definition, underlying pathophysiology and clinical implications.

Classification	Definition	Pathophysiology	Clinical management
Poor intrinsic Ultrafiltration At start of PD	Sodium dip at 60 min < 5 mmol/l or sodium sieving ratio <0.07 with 4.25% dextrose PET	• Explanations largely not understood • Potential influence of genetic determinants (e.g. aquaporin expression)	• Careful evaluation and monitoring of fluid volume. • May be associated with fast PSTR • Earlier indicator of ultrafiltration insufficiency than fast PSTR

Morelle et al. PDI 2021

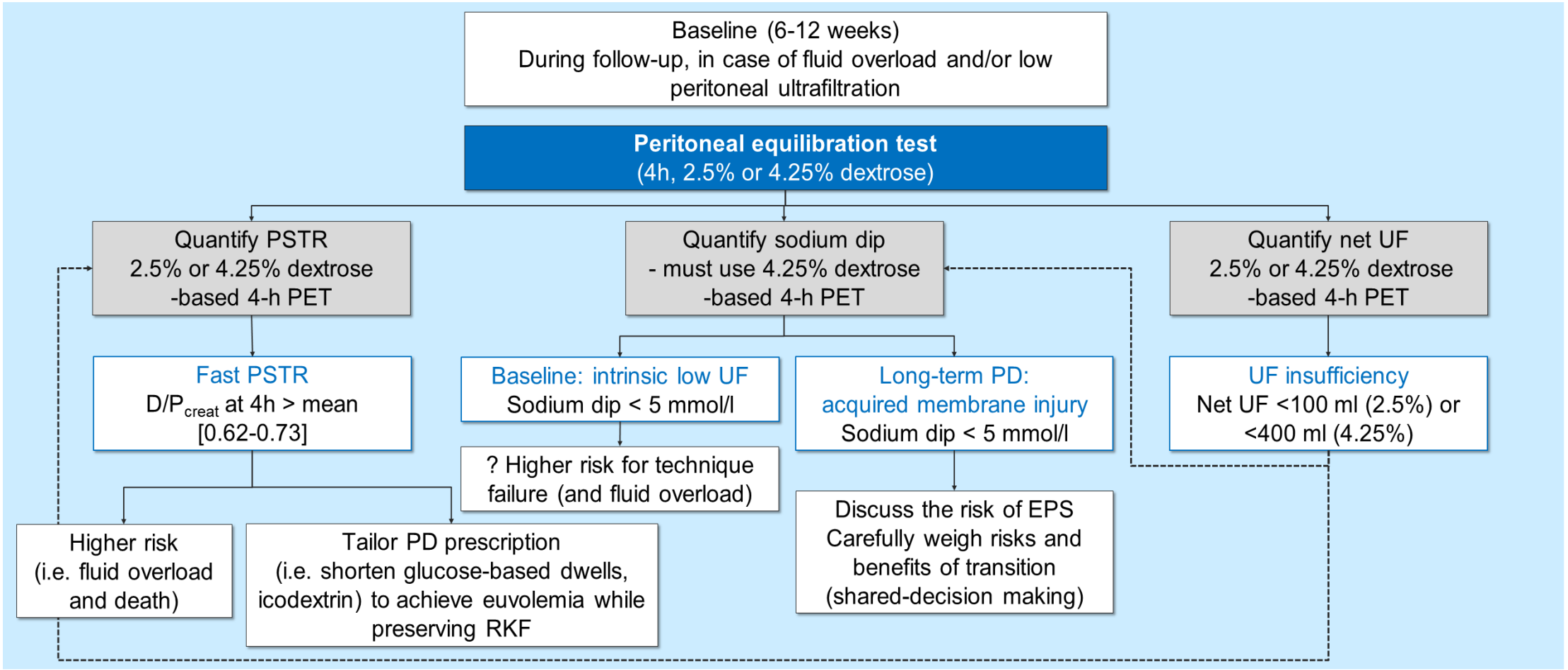
Classification of membrane dysfunction, including definition, underlying pathophysiology and clinical implications.

Classification	Definition	Pathophysiology	Clinical management
Acquired intrinsic ultrafiltration insufficiency Developing over time (years) on PD	Sodium dip at 60 min < 5 mmol/l or sodium sieving ratio <0.07 with 4.25% dextrose PET	• Structural alterations in the peritoneal interstitium in keeping with progressive fibrosis • Usually associated with fast PSTR	Discussion about the potential risks of continuing PD, including EPS, vs. transition to another modality, and shared decision-making with the patient and the PD team

Morelle et al. PDI 2021

ISPD Recommendations for the Evaluation of Peritoneal Membrane Dysfunction in Adults

PERITONEAL DIALYSIS INTERNATIONAL



Johann Morelle, Joanna Stachowska-Pietka, Carl Oberg, et al. **ISPD recommendations for the evaluation of peritoneal membrane dysfunction in adults: Classification, measurement, interpretation and rationale for intervention.** https://doi.org/10.1177/0896860820982218

A 60 -year-old female with ADPKD & DM2 started APD – 2 L fill volume, 4 exchanges over 8 hours. All exchanges 1.5 %

Time since starting PD	Volume status	U/o per day	Total UF per day	Intervention	Outcome
3 months	Fluid overload	700 ml	500 ml	Diuretic 1.5 % & 2.5 % exchanges PET Test –fast PSTR UFc = 500	Responded Daily u/o =900 ml Daily UF=600-800 ml
6 months	Fluid overload	200 ml (PTCA & Urosepsis)	600-800 ml	Diuretic cont. Icodextrin added	Responded Daily UF = 900-1200
1 year	Euvolemic	100-200 ml	800-1000 ml	As above	n/a
18 months	Fluid overload	ANURIC	400-500 ml over last 3 months	UFc = 200 ml Discussions regarding HHD/ IHD and AVF placed at 15 months	• Started HHD training with AVF • Had kidney Tx at 30 months

A 60 -year-old female with ADPKD has recurrent fluid overload since PD initiation and over the course lost residual urine out put

- She likely has early onset of peritoneal membrane dysfunction :**Fast PSTR status**
- Thereafter between 12 months to 18 months demonstrated **Acquired intrinsic ultrafiltration insufficiency (Fast PSTR & low UFc)**
- She likely had **Poor underlying intrinsic Ultrafiltration**
- **Did not measure ”Na dip “**

Volume management in PD patients : Use multifaceted approach

- Dietary education
- Regular assessment of volume status
- Preservation of residual kidney function
- Individualization of PD prescription & interventions according to PD membrane functional status (per ISPD recommendations)

Volume management in PD patients : Multifaceted approach

- When resource constraints prevent the use of routine tests, consideration of membrane function should still be part of the clinical management and may be inferred from the daily UF in response to the prescription. (ISPD practice point)
- Keep the patient engaged in share-decisions
- Proactive approach & plan transition to Hemodialysis (avoid PD centric approach)
- **“ IT IS A JOURNEY – NOT A DESTINATION / NOT A FAILURE ”**

Mortality Trends After Transfer From Peritoneal Dialysis to Hemodialysis

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

Methods and cohort

Incident PD patients transferred to HD (≥ 1 day) between 2000 and 2014

CORR RCITO
n = 5847

ANZ DATA AUSTRALIA & NEW ZEALAND DIALYSIS & TRANSPLANT REGISTRY
n = 6683

USRDS United States Renal Data System
n = 80459

era edta REGISTRY
n = 21574

Results

Mortality rate over first 30-day
(deaths per 100 patients-year)

CORR	68
ANZDATA	48
USRDS	34
ERA	32

Era subgroups

Crude mortality rates were lower for patients transferring in the most recent years (than earlier)

Predictors of mortality

Overall, predictors were consistent across registries

Old age **PD vintage**

Mortality trend

Mortality was highest during the first month and stabilized at 4-6 months in all registries

KI REPORTS
Kidney International Reports

Nadeau-Fredette et al. 2022

Visual abstract by:
Omar Taco, MD MSc

Conclusion: Early period after transfer from PD to HD was associated with a high mortality risk, which was a consistent finding across multi-national registries.

Characteristics of patients who discontinued PD and converted to HD

Kidney360

USRDS

United States Renal Data System

Aged ≥12 years

Newly diagnosed ESKD 2001-2017

Initiated PD during 1st year of ESKD

Discontinued PD 2009-2018

n=232,699 Patients who initiated PD

n=124,213 Patients who discontinued PD

n=68,743 Patients who converted to hemodialysis

Monthly rates of acute care encounters and total costs of care to Medicare sharply increased during the 6 months preceding PD discontinuation

96.2 acute care encounters per 100 patient-months

$20,701 per patient in the last month of PD

Cumulative incidence at 24 months of converting to in-facility HD

3% Home HD initiation

24.8% Death

7.2% Kidney transplantation

Conclusions The transition from PD to HD is characterized by high rates of acute care encounters and health care expenditures. Quality improvement efforts should be aimed at improving transitions and encouraging both home HD and kidney transplantation after PD discontinuation.

Eric D. Weinhandl, Tonya Saffer, Michael Aragon. ***Hidden Costs Associated with Conversion from Peritoneal Dialysis to Hemodialysis***. *Kidney360*. DOI: 10.34067/KID.0007692021

Visual Abstract by Edgar Lerma, MD, FASN