Peritoneal Dialysis Prescription and Modalities

Maria V. DeVita, M.D.
Associate Director Nephrology Lenox Hill Hospital Clinical Associate Professor of Medicine NYU School of Medicine
Meghana Gaiki, M.D.
Fellow, Division of Nephrology, Lenox Hill Hospital
Emmanuelle Gilles, M.D.
Fellow, Division of Nephrology, Lenox Hill Hospital

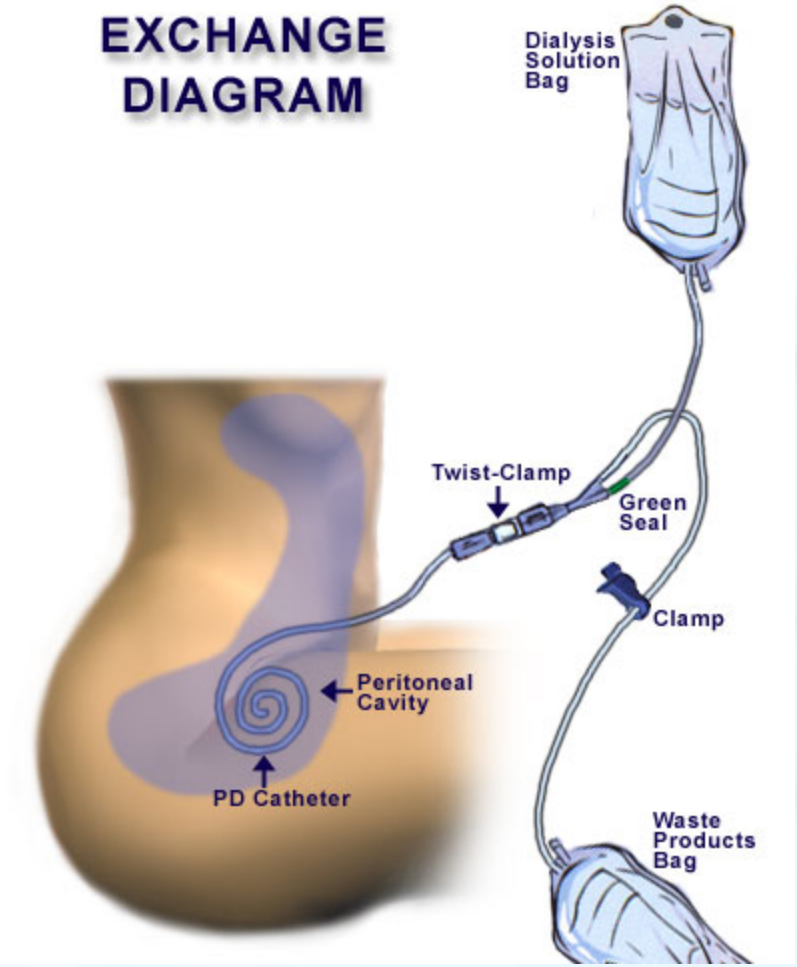
Goals and Objectives

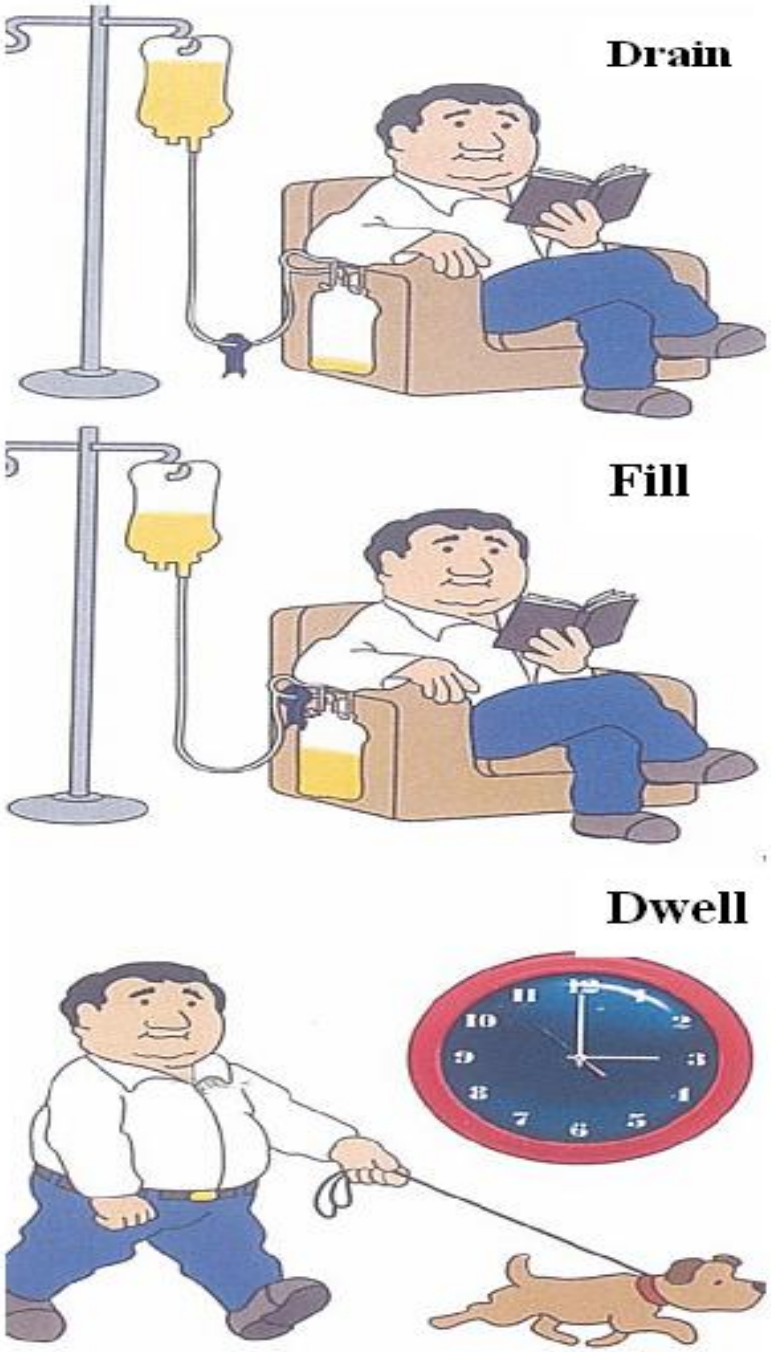
- Introduction to the different modalities of Peritoneal Dialysis (PD).
- Clinical implication of Peritoneal Equilibration Test (PET).
- Chronic Peritoneal Dialysis Prescription.
- Automated versus Ambulatory Peritoneal Dialysis in terms of –
  - Mortality
  - Technique survival
  - Impact on Residual Renal Function(RRF)
  - Volume and blood pressure control

Continuous Ambulatory Peritoneal Dialysis

- In 1976, Popovich et al introduced the concept of continuous ambulatory peritoneal dialysis.
- In 1978, Oreopoulos et al introduced dialysis solutions in plastic bags and use of a single administration tubing for one week.
- In 1980, Buoncristiani et al introduced the ‘ Y ‘ set.
- Now, continuous peritoneal dialysis includes continuous ambulatory and cyclic peritoneal dialysis (CAPD and CCPD)

CAPD


EXCHANGE DIAGRAM
Dialysis Solution Bag
Twist-Clamp
Green Seal
Clamp
Peritoneal Cavity
PD Catheter
Waste Products Bag

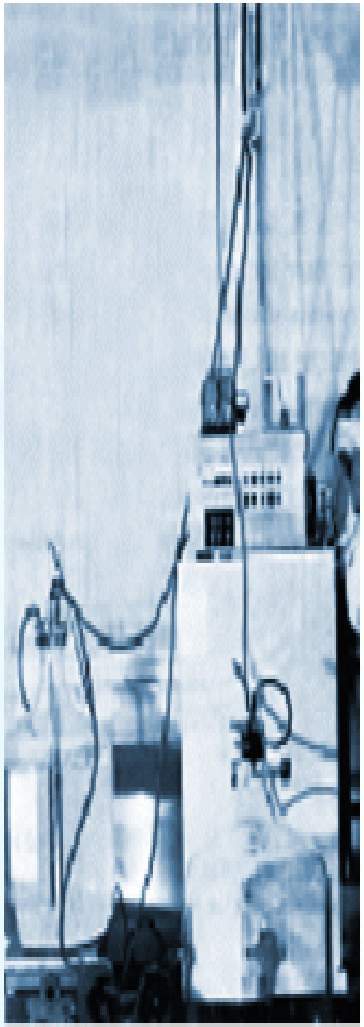

Drain
Fill
Dwell

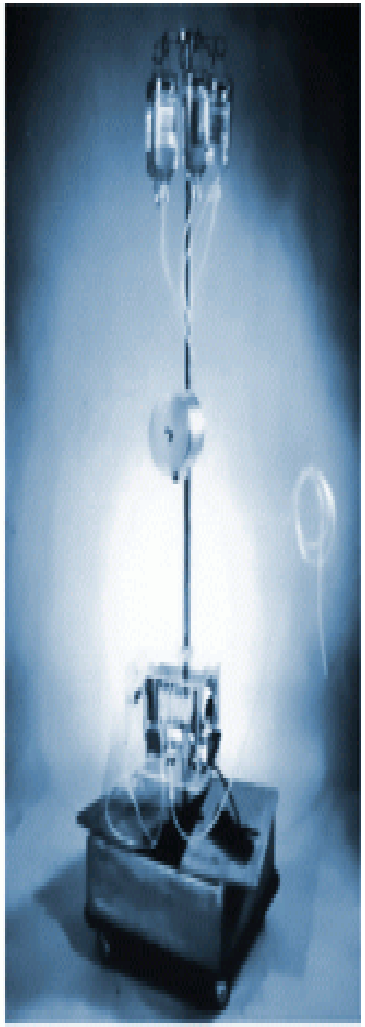
Automated Peritoneal Dialysis

Brenner and Rector's The Kidney, 8th edition, 2008

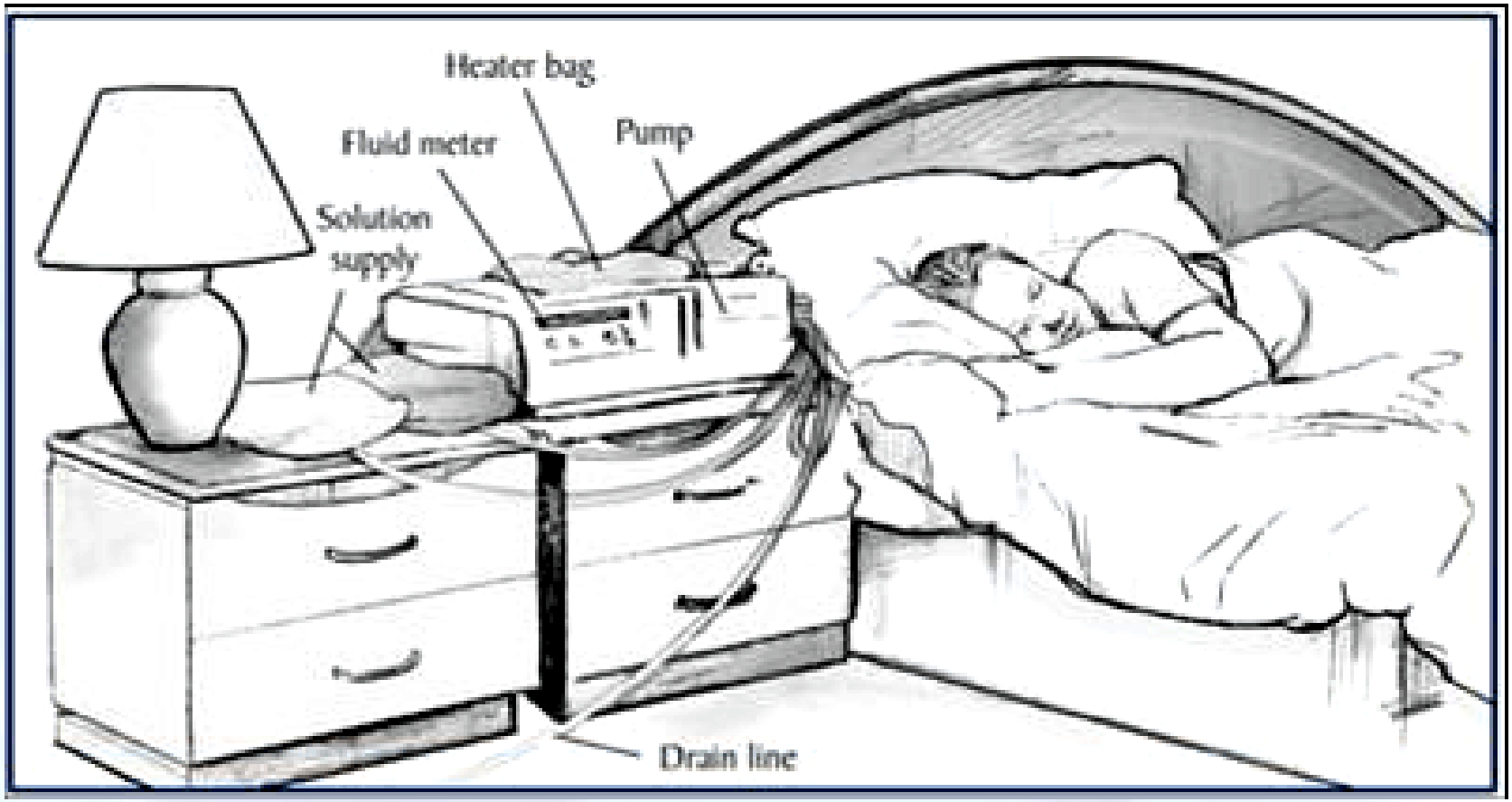
- APD uses a cycler/machine to perform the exchanges.
- For chronic renal failure, APD is traditionally divided into-
  - Continuous cycling peritoneal dialysis/CCPD
  - Nocturnal intermittent peritoneal dialysis/ NIPD.
  - Tidal peritoneal dialysis/ TPD
  - Hybrid Systems.

The First Cyclers





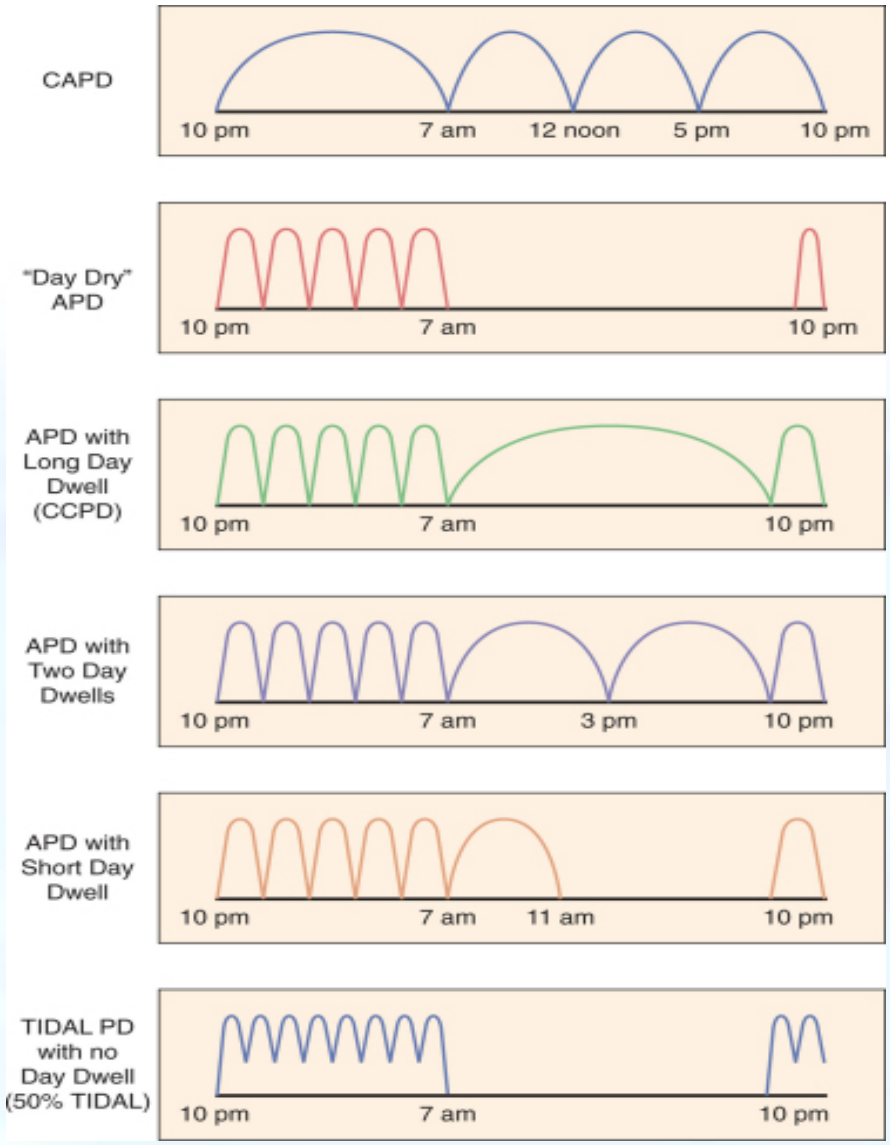
The New Cyclers



The New Cyclers

Modalities of PD

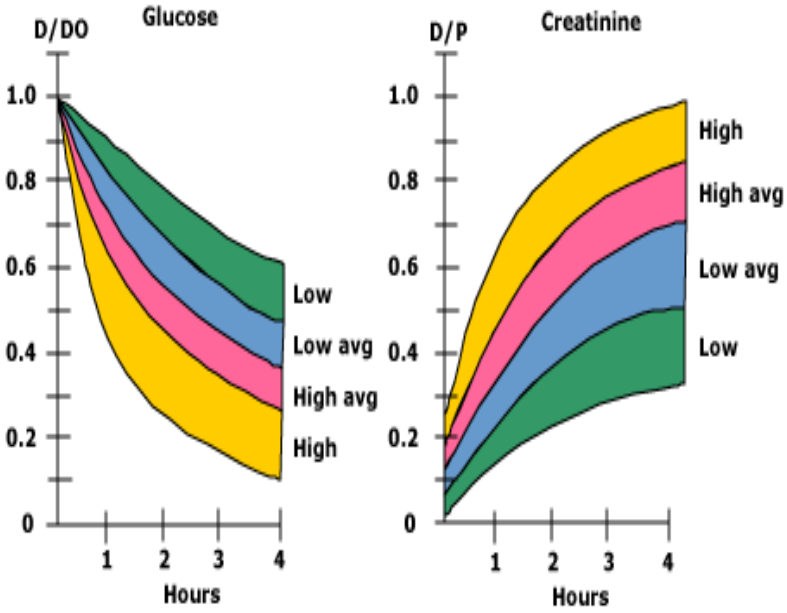
Brenner and Rector's The Kidney, 8th edition, 2008



- Continuous cycled peritoneal dialysis-
  - 3 to 7 cycles of 1.5 to 2.5 L delivered over 9 hours at nighttime.
  - Dwell times range from 45 minutes to 3 hours.
  - Dwell left in at the end of the cycling period and drained out again before the next cycling period about 15 hours later.
- Nocturnal intermittent peritoneal dialysis or day dry APD
  - No day dwell because of good residual renal function or mechanical contraindications.
- High-dose APD or PD plus or APD with 2 day dwells
  - more than one day dwell, requires another exchange sometime during the day.
- APD with short day dwell-
  - leaves some of the day time dry to facilitate ultrafiltration or for comfort or mechanical reasons.
- Tidal PD-
  - Incomplete drain of a proportion of the infused fluid before refilling with the next cycle.
  - Used to minimize down time with a poorly draining catheter or to avoid drain pain.

Interpretation of the PET test

- High transport implies a structural or functional alteration of the peritoneum-
  - A larger effective peritoneal surface area
  - A higher intrinsic membrane permeability (for the rapid equilibration of small solutes including creatinine and urea).
- **High transporters** are prone to lose the osmotic gradient required for sustained ultrafiltration because of rapid absorption of glucose from the dialysate.
  - Subsequent decrease in ultrafiltration capacity
  - Tendency to have greater systemic exposure to glucose than low transporters do.



Clinical implications of transporter type

- High transporters tend to have problems achieving ultrafiltration goals but are efficient with clearance.
- Low transporters tend to achieve ultrafiltration goals but have difficulty with clearance targets.
- Traditionally, high transporters were thought to do best on regimens that involve frequent short duration dwells (APD) maximizing ultrafiltration, and low transporters needed longer dwell times (CAPD) to maximize clearances.

Typical PD Regimens Required to Achieve Adequate Solute Clearances

	Peritoneal Solute Transport Characteristics-D/P Creatinine at 4 Hours			
Patient Body Surface Area (m^2)	Low (<0.5)	Low Average (0.5 to <0.65)	High Average (0.65-0.82)	High (>0.83)
<1.7	CAPD/APD 10-12.5 liters	CAPD/APD+ 10-12.5 liters	APD+* 10-12.5 liters	APD* 10-12.5 liters
1.7-2.0	CAPD+/APD 12.5-15 liters	APD+ 12.5-15 liters	APD+* 12.5-15 liters	APD+* 12.5-15 liters
>2.0	CAPD+,HD	APD+ 15-20 liters	APD+* 15-20 liters	APD+* 15-20 liters

Adapted From Comprehensive Clinical Nephrology- John Feehally, Jurgen Floege, Richard J. Johnson, 3rd edition, 2007.

+ an additional exchange , * use of icodextrin solution .

Peritoneal Dialysis Prescription

Handbook of Dialysis, fourth edition, 2006, John T. Daugirdas, Peter G. Blake, Todd S. Ing

- Clearance Targets-

A consensus target Kt/V for all modalities of PD is 1.7 per week. KDOQI guidelines suggest that peritoneal and renal Kt/V can be added to achieve the target.

Greater residual renal function has repeatedly been shown to be associated with superior survival.

- Incremental versus maximal prescription-
  - In the incremental approach PD is used to make up the differences between residual renal clearance and targeted clearances.
  - In the maximal approach a sufficient prescription of PD is given to meet their targets with PD alone.
- Empirical versus Modeled approach-
  - With the empirical approach a reasonable prescription is chosen and prescription is adjusted to achieve clearance targets.
  - The computer program uses anthropometric data, results of PET test and RRF to predict clearances achieved with various prescriptions.

Factors determining clearance in peritoneal dialysis patients

Handbook of Dialysis, fourth edition, 2006, John T. Daugirdas, Peter G. Blake, Todd S. Ing

- Nonprescription factors-
  - Residual renal function
  - Body size
  - Peritoneal transport characteristics
- Prescription factors-
  - CAPD- frequency of exchanges, dwell volumes, tonicity of dialysis solution.
  - APD- Number of day dwells, volume of day dwells, tonicity of day dwells, time on cycler, cycle frequency, cycler dwell volumes and tonicity of cycler solution.

Typical CAPD Prescription

Handbook of Dialysis, fourth edition, 2006, John T. Daugirdas, Peter G. Blake, Todd S. Ing

1) **Dwell Volumes and Frequency of daily exchanges**

   4 (number of exchanges) x 2L (dwell volumes) is the typical prescription.

   4 x 2.5L in larger patients with small RRF or anuric patients who weigh >75 kg.

   3 x 2L in smaller patients or in patients with good RRF.

   Problems of increasing dwell volumes- back pain, abdominal distension and even shortness of breath.

   Increasing frequency of dwells is less effective than increased volumes for improvement of creatinine clearance as equilibration curve for creatinine is rising 4 hours after the dwell. It is also more expensive and may interfere with patient's lifestyle.

2) **Increasing tonicity of dialysis solution** increases both ultrafiltration and clearance but may lead to hyperglycemia, hyperlipidemia, obesity and long term peritoneal membrane damage.

Typical APD Prescription

Handbook of Dialysis, fourth edition, 2006, John T. Daugirdas, Peter G. Blake, Todd S. Ing

- **Number of day dwells-** Can start with NIPD if patient has good residual volume. Adding a day dwell increases Kt/V by 25%. In high transporters a long day dwell can result in net fluid absorption. This can be countered by shortening the day dwell.
- **Tonicity of day dwells**- Net fluid absorption occurring in day dwells can be countered by using icodextrin dialysis solutions.
- **Time on cycler** – 8 to 10 hrs. The longer the time the patient spends on the cycler the better the clearance.
- **Cycle frequency-** 3 to 5 cycles per 9 hour cycling session. Each cycle lasting 1.5 to 3 hrs. More frequent cycles increases clearance, but a greater proportion of the time is spent draining and filling. Some dialysis time is lost.
- **Cycler dwell volumes** - 2 to 2.5 L. As patients are supine in APD they can tolerate larger dwell volumes more easily. A typical starting volume is 10 to 15 l depending on the patient size.
- **Tonicity of cycler solution**- As with CAPD increasing tonicity increases ultrafiltration , but the same concerns about glucose related complications arise.

Factors taken into account before choosing PD modality

In the past

- Long term outcomes
  - Technique failure
  - Mortality
  - Volume and BP Control
- Residual Renal Function.
- Risk of peritonitis.
- Transporter Status.
- Patient preference.

Current thinking

- **Patient preference.**
- Transporter status?

Increasing use of APD

Mehrotra et al, Kidney Int 2009; 76,97-107

- In the 1980s and early 1990s APD was largely used to optimize volume status in high average and high transporters.
- With the advent of smaller, portable machines; APD use has increased due to physician and patient choice, irrespective of the transport type.
- Percentage of patients on PD using APD in different countries-
  - 59%: US (2007)
  - 60%: Belgium, Denmark and Finland 60%
  - 42%: Australia and New Zealand.

CAPD versus APD

Mehrotra et al, Kidney Int 2009; 76,97-107

- Since 1996, the 1 year mortality outcomes have improved for PD but remained the same for maintenance HD.
- Reasons
  - Decrease in infectious complications.
  - Publication of clinical practice guidelines that may improve prescription management.
  - Increased use of APD- Lower rates of peritonitis with APD.
- APD also associated with-
  - Lower daily sodium removal. (worse volume and BP control)
  - Rapid loss of residual renal function.
  - Higher protein losses with multiple night time exchanges.
  - More expensive

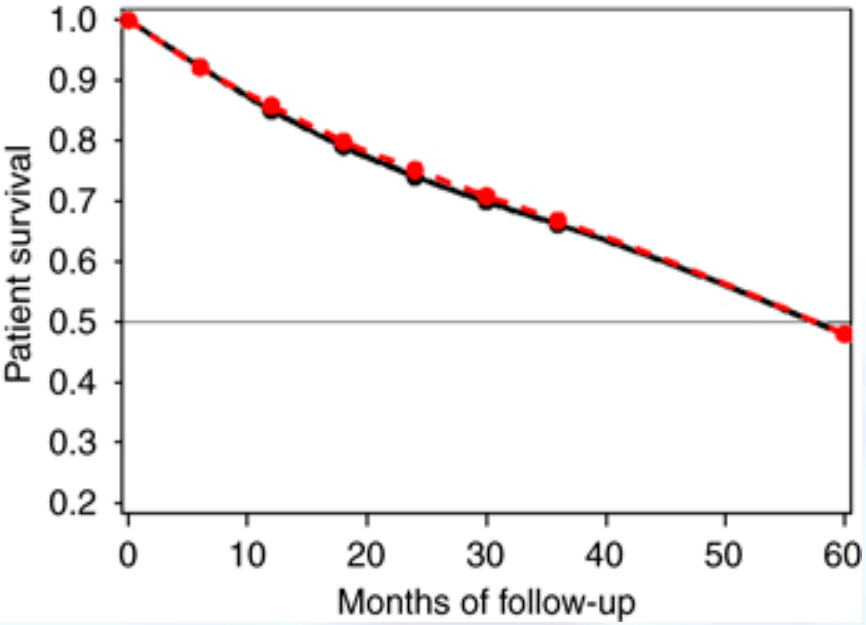
CAPD versus APD

Mehrotra et al, Kidney Int 2009:76,97-107

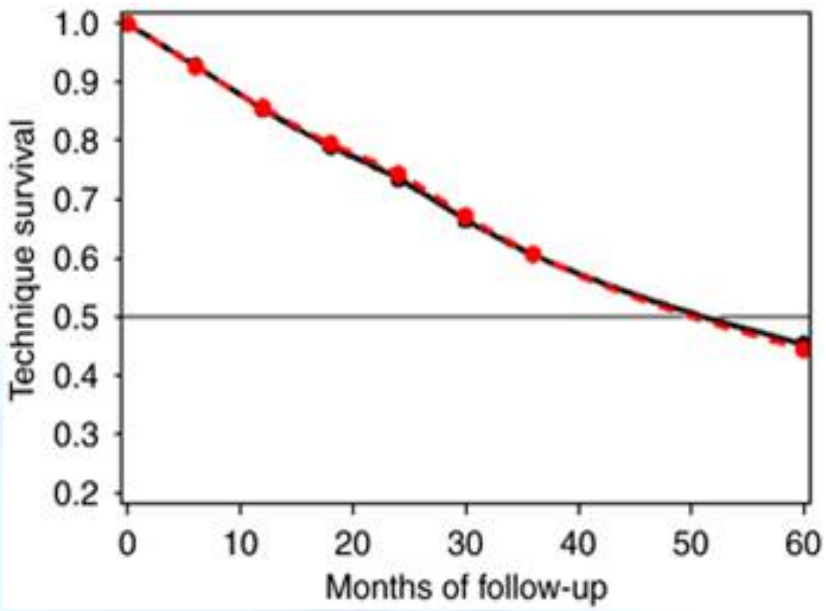
- These differences highlight the need to compare outcomes of CAPD and APD.
- Data from USRDS on 66,381 incident patients on chronic PD from 1996 to 2004 was used.
- The risk of death and technique failure between the two modalities was compared.
- Also wanted to study the impact of APD on the improved outcomes in PD.
- The adjusted median life expectancy improved by approximately 8 years from 1996–1998 to 1999-2001, irrespective of the modality of PD.

The outcomes of continuous ambulatory and automated peritoneal dialysis are similar

Mehrotra et al, Kidney Int 2009; 76,97-107



There were **no significant differences** in adjusted **mortality rates** in patients treated with **CAPD or APD** for virtually all the time periods examined



There were **no significant differences** in either time dependent or overall relative risk **for technique failure between CAPD and APD patients**

Conclusions

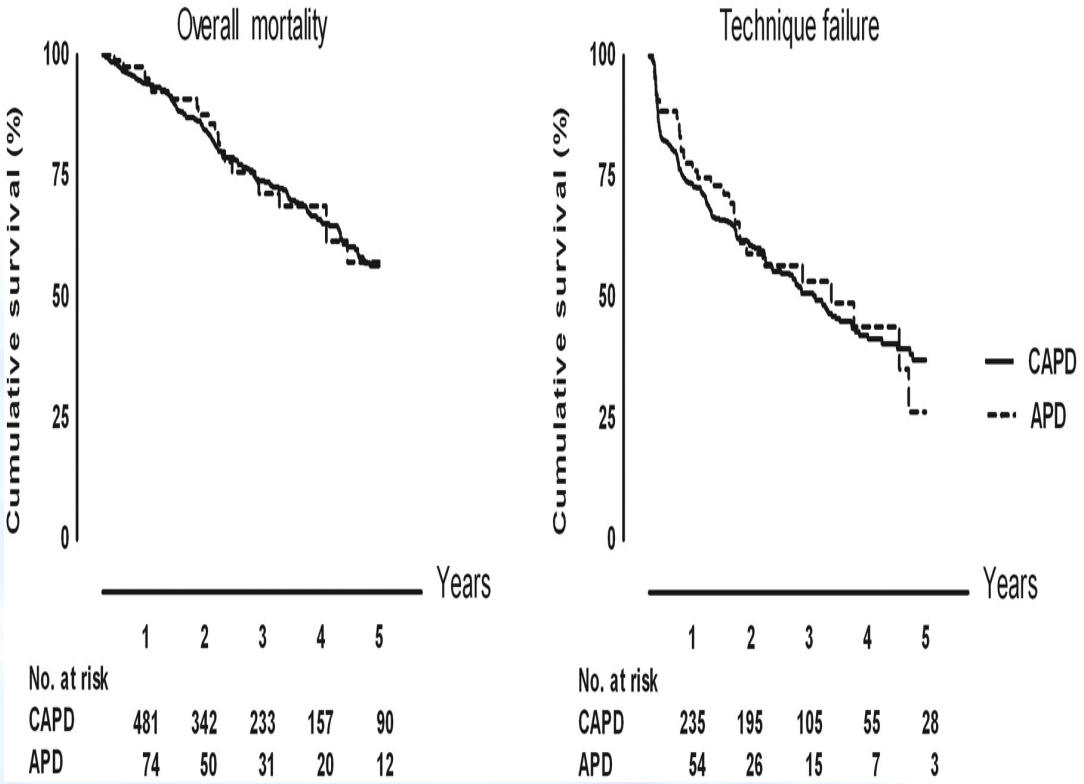
- There have been substantial reductions in the adjusted risk for death and technique failure among incident PD patients since 1996.
- The outcomes of CAPD and APD patients are remarkably similar and the improvement in PD outcomes cannot be attributed to a greater use of APD.
- Centers with a higher PD utilization had a significantly lower risk of technique failure and marginally lower risk of death.

NECOSAD Study Group

Michels WM et al

Clin J Am Soc Nephrol 2009; 4: 943-949

- ❖Netherlands Cooperative Study on the Adequacy of Dialysis.
- ❖ Prospective, Multicenter cohort of ESRD patients (562 on CAPD and 87 on APD)
- ❖Patient preference main reason to be on APD.
- ❖No short-term or long term effect of PD modality on overall mortality or technique failure
- ❖Findings similar to the ANZDATA registry.
- ❖Two large observational studies showed survival benefit with APD.
- ❖The choice to start APD versus CAPD should be based on factors such as quality of life, partner's preference or available resources.



Sodium Removal in Patients Undergoing CAPD and APD

Rodriguez-Carmona A et al, *Perit Dial Int* 2002; 22:705–713

- Study in three steps. Cross-sectional observational (Study A), and longitudinal interventional (Studies B and C).
  - Study A was a cross-sectional survey of Na removal in 63 patients on CAPD and 78 patients on APD.
  - Study B- studied Na removal in 32 patients before and after changing from CAPD to APD therapy.
  - Study C analyzed the impact on Na removal of introducing icodextrin for the long dwell in 16 patients undergoing CAPD or APD.
- Standard APD schedules are frequently associated with poor Na removal rates.
- For any degree of ultrafiltration, Na removal is better in CAPD than in APD.
- Icodextrin, supplementary diurnal exchanges, and longer nocturnal dwell times improve Na removal in APD.
- Patients on APD may have more frequent hypertension because of lower sodium removal.
  - Sodium sieving in the short duration dwells of APD.
  - Less ultrafiltration in the long duration day dwells.

Blood Pressure, Volume and Sodium Control in an Automated Peritoneal Dialysis Population.

Boudville NC et al, Perit Dial Int 2007; 27:537–543

- An observational cross-sectional study with 56 APD patients using icodextrin assessed sodium removal with APD and its association with BP and volume control.

- Mean total sodium removal was 102.9 ± 64.6 mmol/day. 68% had a sodium removal of >120 mmol/day.

- Total sodium removal correlated with total body water (TBW), extracellular water (ECW) and intracellular water (ICW).
- No significant correlation was found between sodium removal and the ECW/ICW ratio in those with sodium removal ≤120 mmol/day compared to those with sodium removal>120 mmol/day.

- Mean SBP 111.9 ± 18.2 mmHg and mean DBP 63.3 ±11.9 mmHg. Only 4 (7%) patients had SBP >140 mmHg and only 1 (2%) had DBP >90 mmHg.
- Blood pressure control was similar in the group of patients with sodium removal ≤120 mmol/day compared to those with >120 mmol/day.

Impact of PD modality on residual renal function

Long term outcomes in automated peritoneal dialysis: Similar or better than in continuous ambulatory peritoneal dialysis?

Mehrotra R, *Perit Dial Int 2009;* 29(S2):111-114

- Faster decline of RRF in APD patients : four single-center observational studies (103 CAPD *and* 108 APD subjects in total)
- Numerous other studies have been unable to demonstrate a more rapid loss of RRF in APD patients (1141 CAPD *and* 484 APD subjects total). Three of those studies were large multicenter trials.
- There is probably **no difference in the rate of loss of RRF between CAPD and APD patients.**

Predictors of Loss of Residual Renal Function among New Dialysis Patients

Moist LM, *J Am Soc Nephrol* 2000; 11:556-564

- The Dialysis Morbidity and Mortality Study (DMMS) is a U.S. Renal Data System (USRDS) special study, including more than 20,000 randomly selected dialysis patients. (HD and PD)
- The study included 33 baseline variables for evaluation as possible independent predictors of residual renal function.
- Loss of residual renal function was defined as an estimated urine output <200 ml/24h at the time of follow-up (8 to 18 mo from initiation of dialysis).
- Patients receiving treatment with PD had a reduced risk of RRF loss when compared to HD-treated patients
- Factors associated with increased loss of RRF on PD-
  - Increasing duration of time on PD, higher eGFR at time of initiation of PD, female gender, Non-white race , presence of DM and CHF were all associated with loss of residual renal function.
- Lower risk of loss of RRF among ESRD patients on PD being treated with ACE inhibitors and/or calcium channel blockers.
- No significant difference in loss of RRF by PD modality type

Impact of PD modality on Peritonitis rates

Long term outcomes in automated peritoneal dialysis: Similar or better than in continuous ambulatory peritoneal dialysis? *Perit Dial **Int*** 29(Supplement 2): 111-114 2009

- Single center nonr**and**omized observational studies showed that APD patients had significantly lower peritonitis rates than CAPD patients did .
- In a recent meta-analysis of data from two r**and**omized controlled trials APD patients had a 46% lower peritonitis rate compared to CAPD.
- Data seems to suggest that APD patients may experience lower peritonitis rates than CAPD patients do.
- Use of connection-assist devices to spike the cycler bags is probably important to maintain this advantage in favor of APD.
- Use of CAPD twin-bag systems **and** of exit-site antibiotic prophylaxis are far more important in lowering peritonitis rates in a PD program than is a greater use of APD.

PD modality and Technique Success

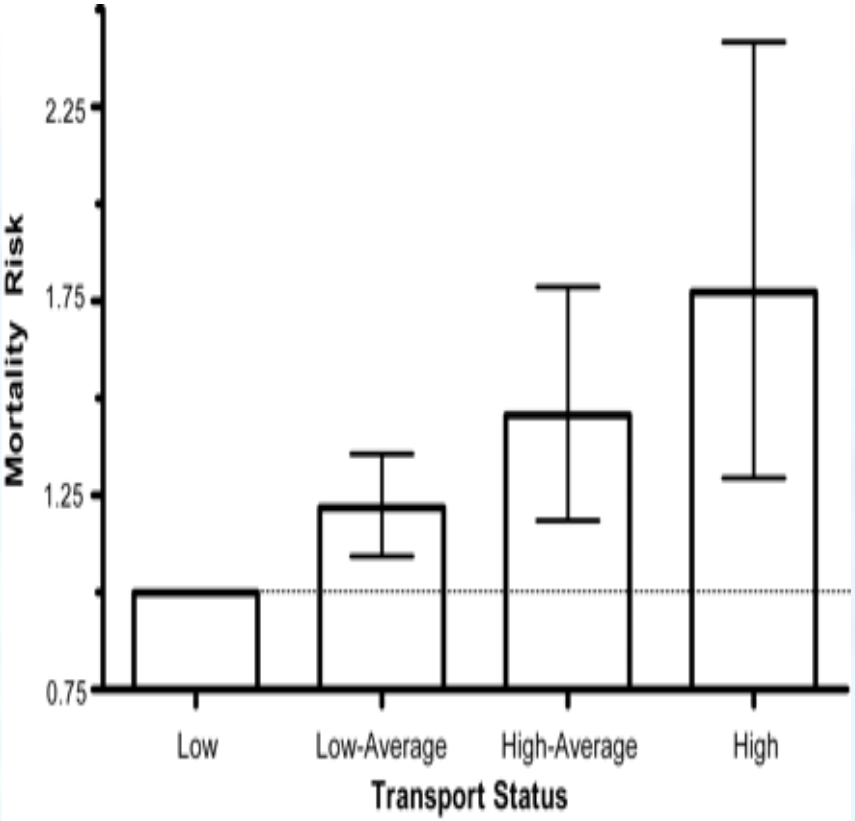
Mehrotra, *Perit Dial Int* 2009; 29(S2):111-114

- "Technique success" is defined as the proportion of patients who did not need to transfer to HD.
- Two randomized controlled clinical trials – underpowered.
- Three observational studies-
  - Two of these (one each from the United States and Mexico) have shown better technique success with APD.
  - The ANZDATA registry (Australia and New Zealand**)** was unable to demonstrate any difference in technique success.
- In the largest study with 40,869 patients , APD had a lower incidence of transfer to maintenance hemodialysis for a variety of reasons:
  - A lower chance of transfer secondary to infection
  - Catheter problem
  - Adequacy considerations
  - Other medical reasons
  - Psychosocial causes However,
  - **The advantage of higher technique success with APD was limited to the first year of therapy**

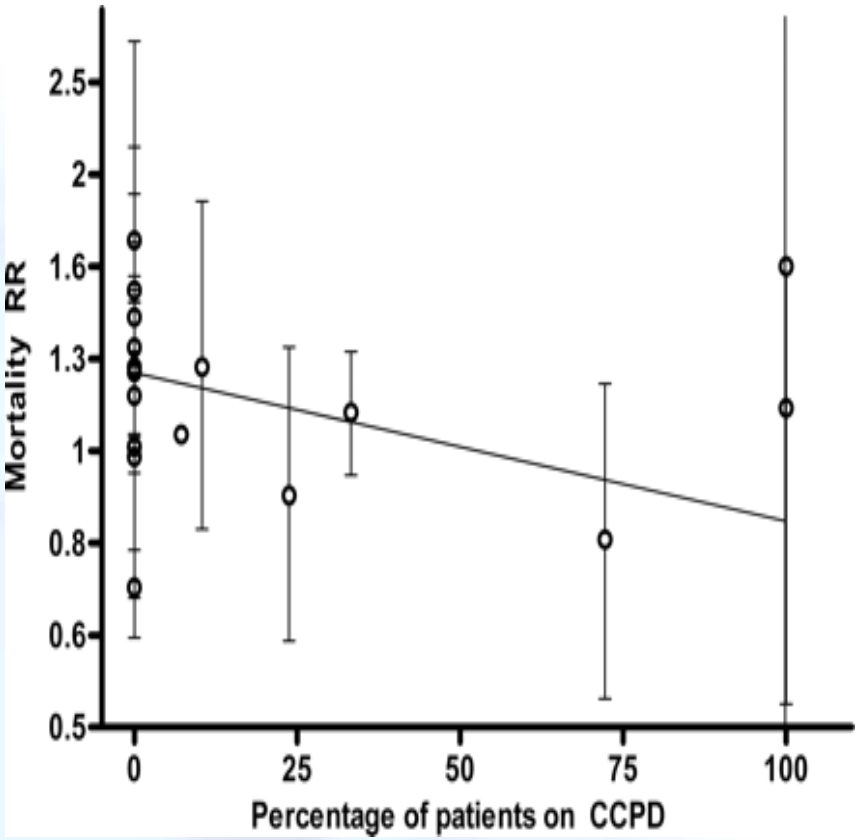
Meta-Analysis: Peritoneal Membrane Transport, Mortality, and Technique Failure in Peritoneal Dialysis

Brimble et al, *J* Am Soc Nephrol 2006 ;(17): 2591-2598.

Increasing peritoneal membrane solute transport rate was associated with an increasing risk for mortality with a trend to increased technique failure.



Use of CCPD seemed to offset some of this negative effect on mortality.

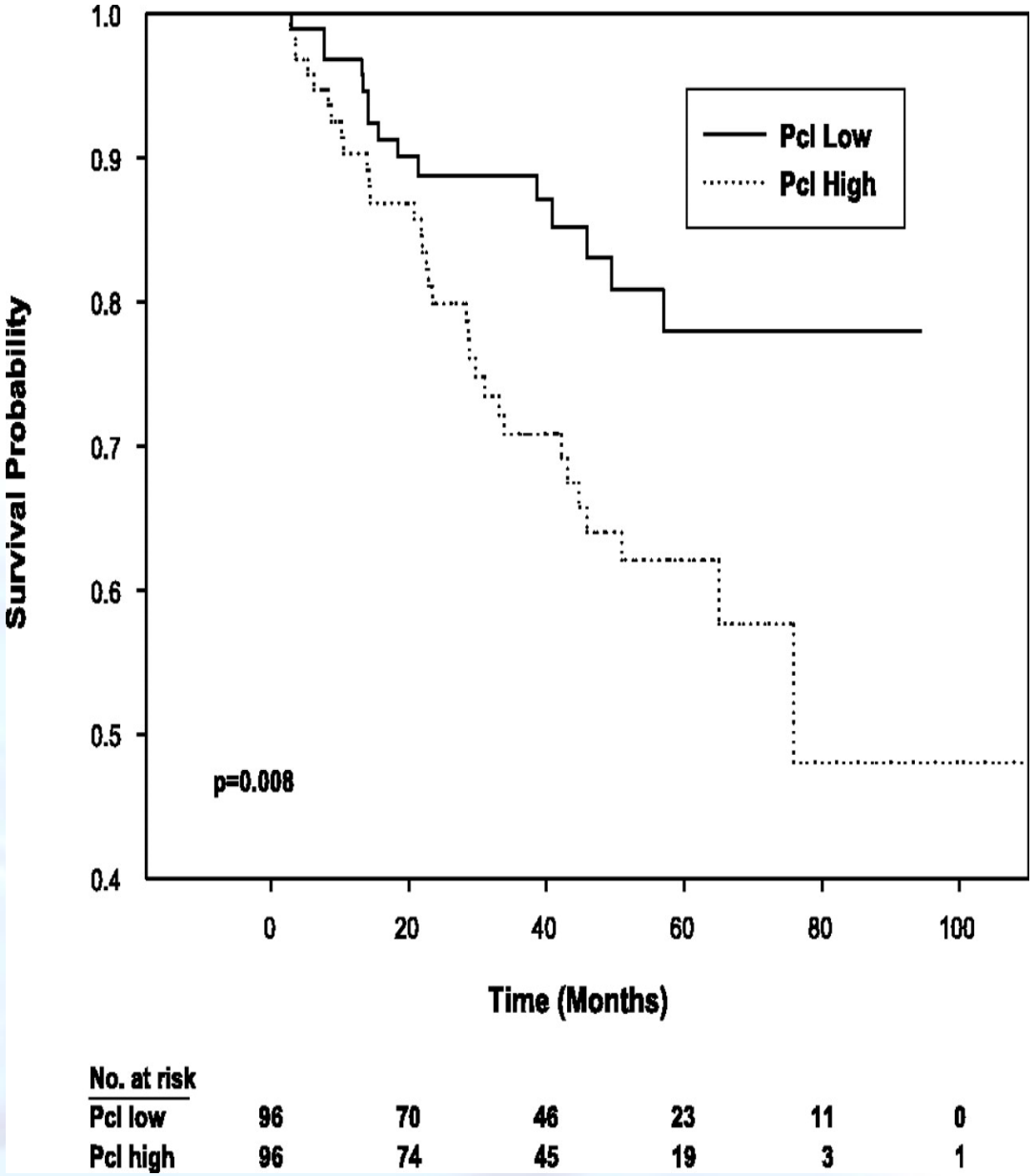


Peritoneal Protein Clearance and not Peritoneal Membrane Transport Status Predicts Survival

A prospective, single-center cohort study by Perl J et al in 192 PD patients suggested that increased peritoneal protein clearance (Pcl) at the start of PD therapy, age and comorbidity grade were predictors of death, independent of baseline small solute transport status.

Patients with baseline Pcl values were included in the study (192 /341).They had higher baseline small solute clearance and greater initial use of APD.

Even after inclusion of all 341 patients, transport status (D/Pcr) did not remain a predictor of survival on unadjusted analysis.



Perl J et al. CJASN 2009;4:1201-1206

Problems Faced by High Transporters

Kam-Tao LI P et al, *Perit Dial Int* 2007; 27(S2): 148-152

- Ultra-Filtration problems
- Hypoalbuminemia
- Rapid satiety
- Marker for inflammation
  - Canusa Study
    - The relative risk of technique failure or death for high vs. low transporters was 4.
  - ANZDATA Registry subanalysis
    - High transport status is independently predictive of death-censored technique failure for patients on CAPD, but not for those on APD.
  - Meta-Analysis of 19 studies
    - High transporters were estimated to have a 77% higher risk for mortality after adjusting for age, diabetes & albumin.

Modeling Prescription for High Transport Status

MAXIMIZING THE SUCCESS OF PERITONEAL DIALYSIS IN HIGH TRANSPORTERS
Philip Kam-Tao Li and Kai Ming Chow , *Perit Dial Int* 2007:27(S2): 148-152

- Frequent, Shorter dwell times- APD
  - The osmotic gradient is dissipated after excessive dwell time. Short dwell times as used in APD maximize small solute clearance and net ultrafiltration.
  - Use of short-dwell therapy at night or NIPD keeps a dry abdomen during the day thus minimizing protein losses not attributable to glucose absorption.
- Use of icodextrin-containing PD solution to achieve volume control in high transporters.
- The association of survival disadvantage and high transport status is confined to patients on CAPD and does not appear to affect those on APD.

Automated Peritoneal Dialysis: A spanish Multicenter Study

Rodriguez A, *Nephrol Dial transplant* 1998; 13:2335-2340

Table 3. Peritoneal urea clearance (l/week) in relation to the transport category

	CAPD	CCPD	TPD (tidal 50%)	TPD (tidal 25%)
All patients	55.40±8.76	74.82±12.62	69.20±14.63	66.89±13.23
Kt/V	1.51±0.32	2.03±0.39	1.88±0.35	1.80±0.40
At night time		61.38±12.2	56.45±13.53	53.19±11.33
Transport category				
High	60.58±3.51	84.51±10.43	80.04±13.02	68.78±20.26
High–average	55.12±10.7	75.78±14.27	71.58±20.20	69.39±15.02
Low–average	53.78±8.29	71.55±10.79	67.40±9.34	72.07±5.52
Low	56.28±7.32	73.01±12.59	65.36±14.26	64.85±7.01

High *vs* low–average, $P<0.001$; high *vs* low, $P<0.01$; high–average *vs* low–average, $P<0.05$.

Table 4. Peritoneal creatinine clearance (l/week/1.73 m^2) in relation to the transport category

	CAPD	CCPD	TPD (tidal 50%)	TPD (tidal 25%)
All patients	42.80±9.95	52.19±11.11	51.31±13.35	49.17±11.83
At night time		40.80±11.09	39.94±12.88	37.22±10.57
Transport category				
High	61.53±4.04	66.44±8.35	69.09±20.98	66.75±22.46
High–average	45.35±10.71	53.71±9.67	53.69±7.05	51.08±6.7
Low–average	43.77±5.9	50.37±10.32	49.54±9.66	48.13±10.53
Low	32.77±9.16	44.67±8.49	40.31±10.11	41.37±7.94

High *vs* other categories, $P<0.001$; high–average *vs* low–average, $P<0.05$; high–average *vs* low, $P<0.001$; low–average *vs* low, $P<0.001$.

Patient Preference

QUALITY OF LIFE IN AUTOMATED AND CONTINUOUS AMBULATORY PERITONEAL DIALYSIS. Michels et al.
Perit Dial Int. 2011 Mar;31(2):138-147

- Advantages of CAPD
  - Cheaper
  - Freedom from machine
  - Easier to be trained.
- Advantages of APD
  - More time available for work, family and social activities as most of the fluid exchanges are at night.

- In a recent study, Michels et al used the prospective cohort of the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD) and showed **no differences in quality of life between patients starting on CAPD versus APD.**

Summary

- Thus all evidence so far seems to suggest that the **choice of the initial PD modality should be based on patient preference**, as neither modality has any advantage over the other in terms of survival advantage, preserving renal function, technique success, risk of peritonitis or blood pressure control.
- APD is associated with lower risk of transfer to maintainence hemodialysis early during the course of renal replacement.
- There is data suggesting that APD may have a survival advantage over CAPD in high transporters, but newer data suggests that the peritoneal protein clearance and not the peritoneal membrane transport status may predict survival outcomes.
- Choice of PD modality should mainly be based on Patient preferences.

Additional References

Brenner and Rector's The Kidney, 8th ed.

Comprehensive Clinical Nephrology- John Feehally, Jurgen Floege, Richard J. Johnson,

3rd edition, 2007.

Burkart JM Effect of peritoneal dialysis prescription and peritoneal membrane transport characteristics on nutritional status, *Perit. Dial. Int.* 1995; 15(S5):S20-35

Churchill DN, Thorpe KE, Nolph KD, Keshaviah PF, Oreopoulos DG, Pagé D, Increased peritoneal membrane transport is associated with decreased patient and technique survival for continuous peritoneal dialysis patients. (CANUSA); *J Am Soc Nephrol* 1998; 9 :1285-92.

Badve SV, Hawley CM, Mcdonald SP, Mudge DW, et al, for The ANZDATA Registry PD Working Group. Automated and continuous ambulatory peritoneal dialysis have similar outcomes *Kidney Int* 2008; 73:480-488

Google.com-images

Question 1

- A 44yo African-American woman has CKD-stage 5 due to hypertension and diabetes mellitus. She is on a kidney transplant list, but has no living donor. She has decided to proceed with peritoneal dialysis but is concerned for her overall health and well-being. She wants to know if it is better to proceed with CAPD or APD. You advise her that:

- A. Patients who undergo CAPD are at a higher risk for death and technique failure than APD patients
- B. Patients who undergo CAPD are at a lower risk for death and technique failure than APD patients.
- C. Both CAPD and APD patients have a high risk for technique failure and transfer to hemodialysis.
- D. There is no difference in risk of death or technique failure in CAPD patients when compared to APD patients.

Correct Answer: D

Shown in Mehrotra et al. KI 2009 (slides 20 and 21) When analysis subdivided into earlier and more recent cohorts, no differences were found between the 2 PD techniques.

Question 2

- In the above patient, factors that will increase her rate of loss of residual renal function include all but:

- A. Gender
- B. Ethnicity
- C. Use of PD instead of HD
- D. Use of APD instead of CAPD

Correct Answer: C

Factors associated with an increased loss of residual renal function include female gender, non-white, history of diabetes, history of CHF. There is no effect of PD modality on rate of loss of residual renal function (e.g. CAPD and APD are equal). Patients on PD have a slower rate of change in RRF.