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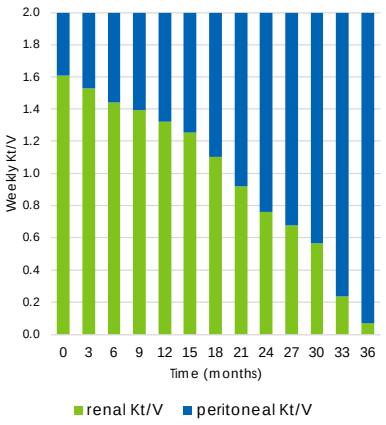

Incremental Peritoneal Dialysis

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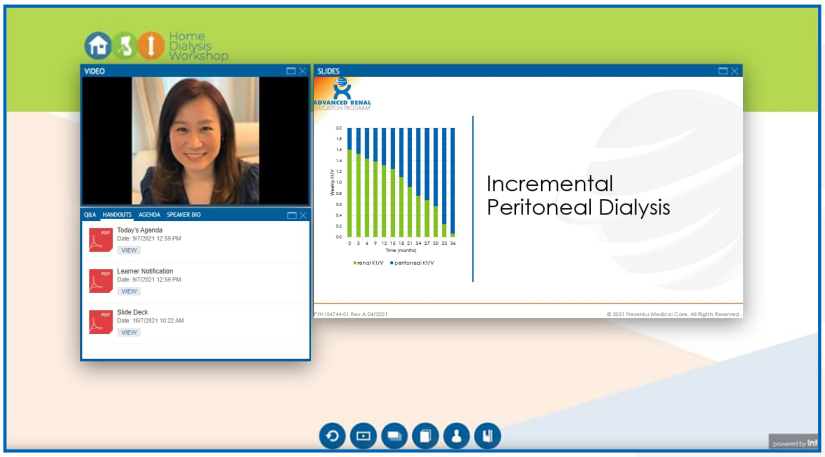

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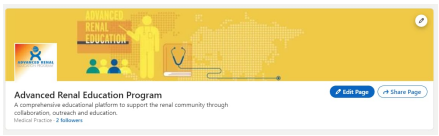

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ADVANCED RENAL EDUCATION PROGRAM

Home Dialysis Workshop
Webinar Series

Clinical Considerations and Applications of Incremental PD

Thursday, March 3, 2022
12:00 PM – 2:00 PM, ET

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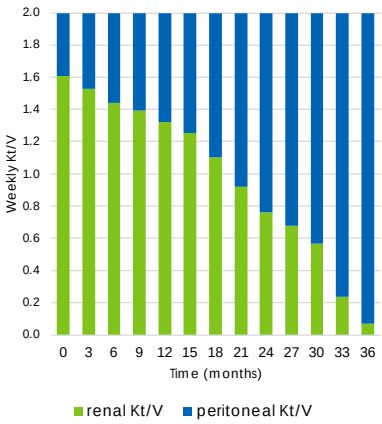

Incremental Peritoneal Dialysis

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Course Objectives

- ✓ Define incremental PD and described its benefits and challenges
- ✓ Understand how to prescribe incremental PD with an emphasis on goal-directed therapy
- ✓ Examine monitoring and intensifying PD prescriptions
- ✓ Review clinical outcomes of incremental PD

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Polling Question

How is incremental PD defined today?

A. Strategy where PD is started earlier, but at lower than "full-dose" therapy

B. Strategy by which a less than standard "full-dose" PD is prescribed in patients initiating PD

C. Strategy where patients do not perform PD every day

Incident PD Patients

PD patients often initiate therapy with significant residual kidney function (RKF)[1]

"The presence of residual kidney function at the start of PD may enable individuals to start on a low dose prescription that may be increased incrementally as residual kidney function declines or as clinically indicated. This may allow patients more time for life participation, less treatment burden and better quality of life."

- 2020 ISPD Practice Recommendations: Prescribing High-Quality Goal-Directed Peritoneal Dialysis[2]

Mean eGFR of incident PD patients[3]

9.9 ± 3.7

mL/min/1.72m²

N=7,790 Range: 0-30 mL/min/1.72m²
Data from ESRD Medical Evidence Report, 29 Dec 2019 – 4 July 2020, PD as initial modality

The Incremental PD Approach[1]

- Strategy by which a less than standard "full-dose" PD* is prescribed in patients initiating PD, taking RKF into account
- The combination of RKF with prescribed therapy is sufficient to achieve individualized goals
- There is a clear intention to increase the PD prescription, if and when, it becomes necessary – based on close clinical monitoring

*Generally, "full-dose" PD does not consider the contribution of RKF

[1]Blake PG, et al. *Perit Dial Int*. 2020;40(3):320.

Incremental PD is not[1]...

- Done because of financial constraints or because a patient is on a palliative trajectory
- Early start PD, where dialysis is not yet required (e.g., GRF > 15 mL/min/1.73m^2)
- Urgent start PD, which is initiated with low volumes due to risk of leaks and not because of residual kidney function

[1]Blake PG, et al. *Perit Dial Int*. 2020;40(3):320.

Potential Benefits of Incremental PD[1,2]

"Achieve realistic care goals that maximize patient satisfaction and provide high-quality care"

-2020 ISPD Guidelines

- Maintenance of RKF
- "Easier" initial prescription may allow for lower anxiety and stress
- Lower burden may facilitate better adherence
- Lower glucose exposure
- Time to patient to build self-confidence and self-care
- Lower fill volumes have lower IPP, may lead to fewer complications
- Greater participation in life activities
- Fewer daily PD procedures could reduce risk of peritonitis
- Requires less solution and so costs less

Blake PG, et al. Perit Dial Int. 2020;40(3):320
Brown EA, et al. Perit Dial Int. 2020;40(3):244-253

Challenges with Incremental PD

- Necessity of periodic of RKF labs (urine volume and clearance) and regular clinical assessment[1]
- Ensuring initial modality education is clear that the prescription will need to increase as RKF declines[2]
- Multiple prescription changes can be confusing for the patient[3]
- Patient resistance to increasing their prescription[2]
- Risk of underdialysis with rapid, unexpected RKF decline[4]

[1]Blake PG, et al. *Perit Dial Int*. 2020;40(3):320. [2]Reddy YN V, Mendu ML. *Clin J Am Soc Nephrol*. July 2020. [3]Ankawi GA, et al. *Can J Kidney Heal Dis*. 2016;3. [4]Auguste BL, Bargman JM. *Semin Dial*. 2018;31(5):445-448.

Identifying Patients for Incremental PD

- No consensus on characteristics of "ideal" patients for incremental PD
- Patients with RKF can be assessed for incremental PD

Criteria may include*:

- Amount of RKF[1]
- Ability to maintain euvolemia[2]
- Relatively controlled BP, PO_4^{2-}, & K^+
- Clinically stability
- Understanding & consent

*Based on professional judgement of the speakers

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[1]Blake PG, et al. *Perit Dial Int*. 2020;40(3):320
[2]Wang AYM, et al. *Perit Dial Int*. 2020;40(3):282-292

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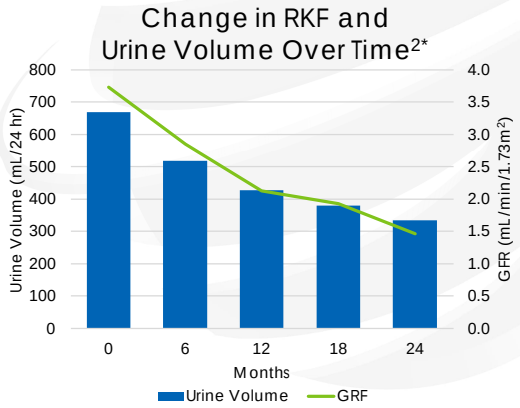
Setting Expectations for Patients

Early education on the eventual need to transition to "full-dose" PD can help overcome barriers to adherence and reduce the risk of technique failure[1]

- ❑ Necessity of regular clinical assessment[1]
- ❑ Ensure patient communication is clear on the prescription needing to increase as RKF declines[1]



*Adapted from Table 1 in Bargman[2]

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[1]Reddy YN V, Mendu ML. *Clin J Am Soc Nephrol*. July 2020
[2]Bargman JM, et al. *J Am Soc Nephrol*. 2001;12(10):2158-2162

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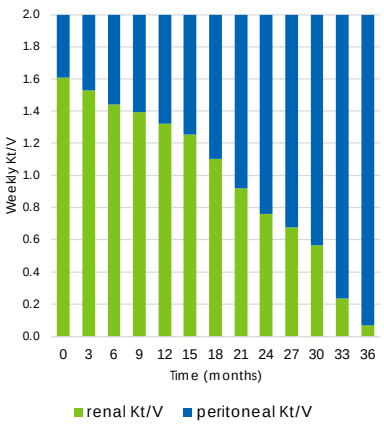

Prescribing & Monitoring Incremental PD

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Case Introduction: Mrs. J

- 76-year-old female patient with renal failure due to glomerulonephritis
- Has been under nephrology care for past 4 years and has had pre-dialysis modality education
- Increasing fatigue, mild edema, slightly elevated K+, ↑AHTs required
- PD catheter was placed, and PD training commenced at the clinic 2 weeks later
- Patient Characteristics
  - Height: 161 cm
  - Weight: 78 kg
  - Urine output: ~500 mL/day
  - eGFR: 5.8 mL/min

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Adequate Peritoneal Dialysis[1]

Fluid balance, BP control, cardiac markers acceptable

Biochemical markers within acceptable ranges

Maximized quality of life

Kt/V

Small solute clearance targets are met

[1]Brown EA, et al. Perit Dial Int. 2020;40(3):244-253

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Mrs. J: PD Therapy Goals

- Quality of Life:
  - ✓ Minimize time on therapy
  - ✓ Maintain sleep quality
  - ✓ Feel good
- Fluid balance, BP control, cardiac markers acceptable
  - ✓ Remove ~500 mL/day UF
  - ✓ Controlled blood pressure
  - ✓ Preserve RKF
- Biochemical markers:
  - ✓ Minimize protein loss
- Adequate clearance
  - ✓ Total Kt/V ≥ 2.0

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Full-Dose vs. Incremental PD[1]

Generic Full-Dose PD Prescriptions

- CAPD: 4 x 2 L
  3 daytime + 1 long overnight dwell
- APD: 10 L/day
  8 L overnight + 2 L last fill

Initial PD prescription in a patient with significant RKF may include:

- CAPD or APD
- Fewer total exchanges
- Lower volume exchanges
- Lower total volume
- Dry periods

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[1]Blake PG, et al. *Perit Dial Int*. 2020;40(3):320.

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What about intermittent PD?

Intermittent PD (<7 days/week) is considered a form of incremental PD[1]

Intermittent PD may not be appropriate for chronic dialysis patients because*:

- Volume control is challenging
- Urea kinetics are complicated
- Risk of hyperphosphatemia
- Potassium control is difficult

Intermittent PD may be appropriate for:

- Elderly patients with substantial comorbidities (in-center IPD)[2]
- Hospitalized patients[3]

*Based on professional judgement of the speakers

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[1]Blake PG, et al. *Perit Dial Int*. 2020;40(3):320. [2]Fourtounas C, et al. *Nephrol Dial Transplant*. 2009;24(10):3215-3218. [3]Pirkle JL. *UpToDate*. 2019;Topic 1858(Version 24.0).

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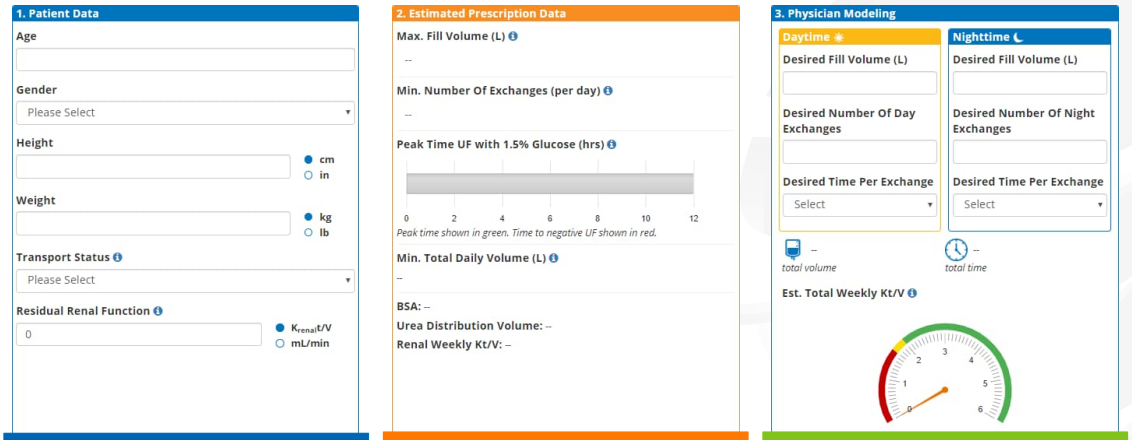
Online PD Calculator



1. Enter basic patient data
- Age, gender, height, weight
- Transport status
- RRF

2. Review estimated data
- Provides general guidance
- Based on modeling assumptions: max fill volume used, 4-hour dwells, continuous therapy, 1 L UF

3. Predict outcomes
- Enter parameters and review modeling results for possible prescription options

https://fresenius.pdcalculator.com/

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Determining Appropriate Dwell Time

Prescribed dwell time should consider:

- Removal requirements for fluid and sodium[1]
- Small solute clearance (Kt/V)[2]
- Patient preference and modality[2]

[1]Wang AYM, et al. *Perit Dial Int*. 2020;40(3):282-292
[2]Brown EA, et al. Perit Dial Int. 2020;40(3):244-253

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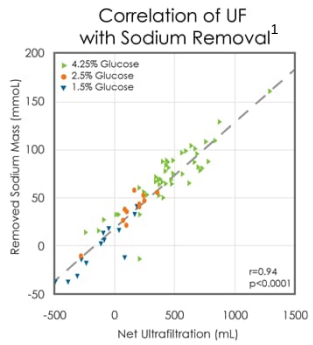
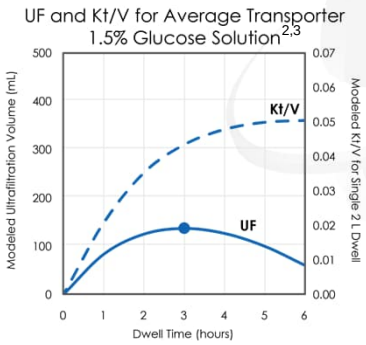
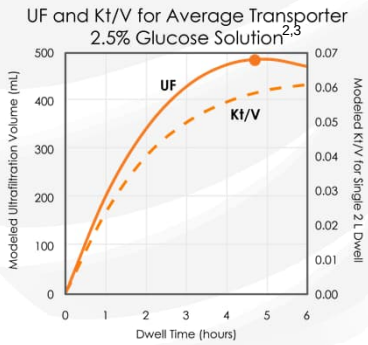
Determining Appropriate Dwell Time

Targeting a dwell time for peak UF is also appropriate for sodium and small solute clearance



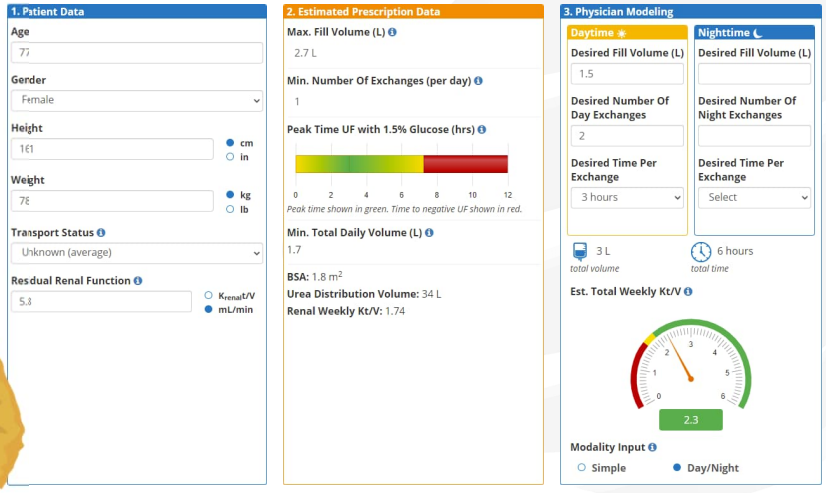




Dwell time between 3 and 5 hours would be appropriate for Mrs. J

[1]Wang T, et al. *Kidney Int*. 1997;52(6):1609-1616. [2]Akonur A, et al. *Perit Dial Int*. 2013;33(6):646-654. [3]Mujais S, Vonesh E. *Kidney Int Suppl*. 2002;(81):S17-S22.

Determining Adequate Clearance



Mrs. J: Initial Incremental PD Prescription

- Manual daytime exchanges (CAPD)
- 2 exchanges per day (dry overnight)
- 3 hours per exchange
- 1.5 L fill volume
- 1.5 or 2.5% dextrose solutions based on weight and BP
- 160 mg BID Lasix
- Estimated Kt/V: 2.3
  - Renal: 1.74
  - Peritoneal: 0.56

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Monitoring the Initial Prescription[1]

Prior to formal laboratory testing, the patient should be assessed for fluid removal and clinical symptoms

- Achieved total fluid removal (UF + urine)
- Changes in body weight
- Clinical signs of overhydration or dehydration
- Clinical signs of increased intraabdominal pressure
- Clinical signs of inadequate clearance (uremic symptoms)
- Thorough comprehensive evaluation of the patient

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[1]K/DOQI . *Am J Kidney Dis.* 2006;48 Suppl 1:S91-S97

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6 weeks later…

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Mrs. J: Laboratory Testing & Clinical Assessment

- PET: Low transporter
- Clearance: Total Kt/V 2.1
  - Renal: 1.62
  - Peritoneal: 0.48
- Fluid balance: slight fluid overload
  - + 1.1 kg
  - ~700 mL/day (300 mL UF) fluid loss
- Labs:
  - BUN: 60 mg/dL
  - Creatinine: 5.5 mg/dL
  - Albumin: 3.9 mg/dL
  - Phosphate:6.0 mg/dL
- QoL: 😐
  - Feeling okay, gets winded sometimes
  - No concerns with therapy burden

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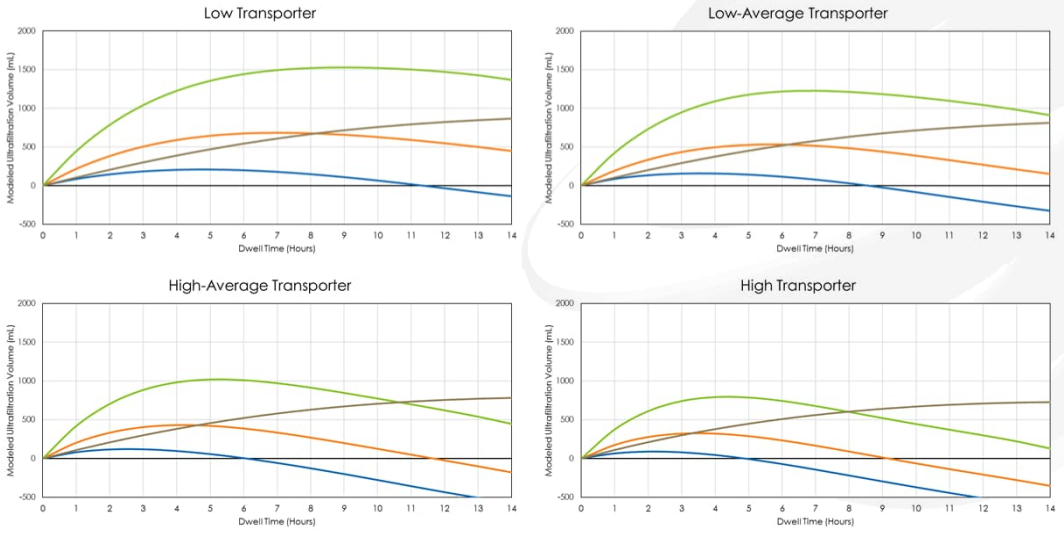
Ultrafiltration Profiles[1]

1.5% Dextrose

2.5% Dextrose

4.25% Dextrose

7.5% Icodextrin



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[1]Mujais S, Vonesh E. *Kidney Int Suppl*. 2002;(81):S17-S22

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How would you adjust Mrs. J's prescription?

A
Increase volume
- 2 x 3 hour-exchange
- 2.0 L fill volume

B
Increase time
- 2 x 5-hour exchanges
- 1.5 L fill volume

C
Increase fill volume & time
- 2 x 5-hour exchanges
- 2.0 L fill volume

D
Switch to cycler
- 3 x 2-hour cycles
- 1.5 L fill volume

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Monitoring Incremental PD[1]

Similar approach to monitoring all PD patients, but with an intent to intensify the prescription as needed

- Quarterly, or more frequently if clinically indicated
- Fluid status: urine volume and UF
- Blood chemistry (BUN, Creat, Phos, Alb)
- 24-hour renal and peritoneal clearance
- Quality of Life
- Other uremic symptoms

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[1]Blake PG, et al. *Perit Dial Int*. 2020;40(3):320.

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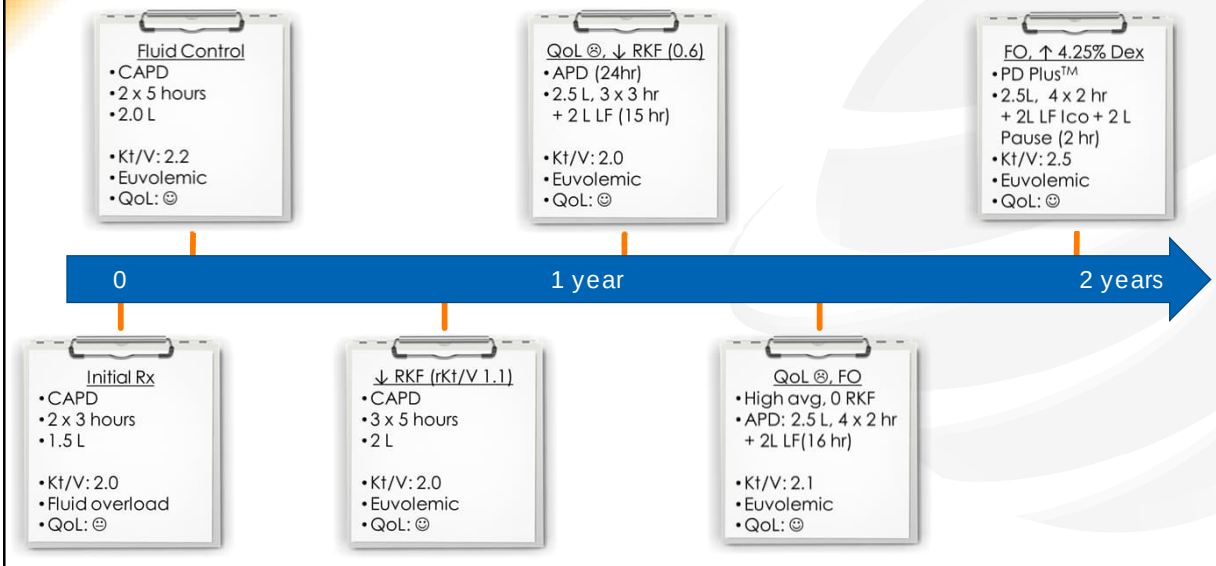
Mrs. J: PD Timeline



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Mrs. J: 1-Year Later

- Continued intensified PD (PD Plus)
  - 24-hour continuous therapy
  - 4 x 2 hours + Ico last fill + 2 L pause exchange
  - Fill Volumes: 2.5 L overnight, 2.0 L during the day
- Maintaining adequacy, ↑ FO, ↑ blood pressure, QoL 😐
- Suspected ultrafiltration failure, later confirmed
- Plans to make a transition to more frequent home HD, AVF placed

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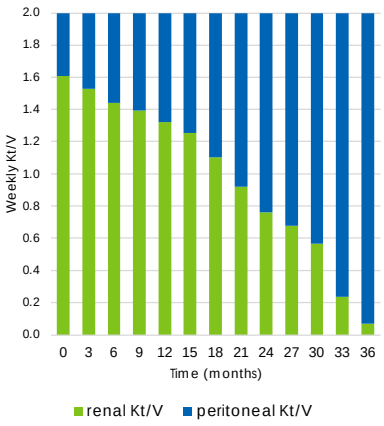

Outcomes of Incremental PD

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Clinical Outcomes of Incremental PD

No solid evidence on the benefits of incremental dialysis have been published. Additional studies are required.

> "In the meantime, and in the absence of definitive evidence as to whether incremental or full-dose dialysis prescription is best, it seems reasonable to advocate an incremental approach."
>
> - 2020 ISPD Practice Recommendations: Incremental Peritoneal Diaysis[2]

Limited analyses suggest[1]:

- Longer preservation of RKF
- No increased risk of mortality
- Defers full-dose PD by 6-19 months

[1]Garofalo C, et al. J Nephrol. 2019;32(5):823-836.
[2]Blake PG, et al. Perit Dial Int. 2020;40(3):320.

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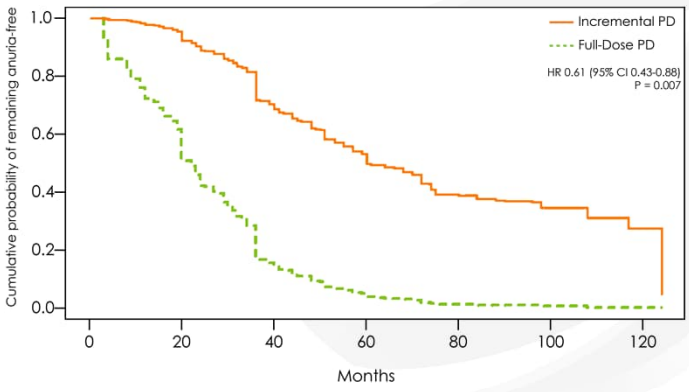
Incremental PD May Preserve RKF[1]

- Single-center, retrospective analysis from Korea, all patients on CAPD
- Comparison between:

Incremental N=176	Full Dose N=171
• 1-2 exchanges/day	• 3+ exchanges/day
• 7 days/week	• 7 days/week
• Total Kt/V > 1.7	• No Kt/V requirement

- *Note: The clinician's decision between full-dose and incremental PD could have been affected by several clinical factors such as RRF, lifestyle, body size, gender, and comorbidities.*

Probability of Remaining Anuria-Free*



*Adapted from Figure 2 in Lee[1]

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[1]Lee Y, et al. *Sci Rep*. 2019;9(1):10105.

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Importance of RKF

The contribution of RKF may be much more important than peritoneal solute clearance[1]

- **0.5** mL/min /1.73m² — Increase in GRF[1]
- **12%** — Decrease in RR of death*
- **250** mL/24 hr — Increase in Urine Volume[1]
- **36%** — Decrease in RR of death‡

Benefits of preserved RKF[2]

- Maintenance of euvolemia
- Better blood pressure control
- Improved nutritional status
- Reduced erythropoietin requirements
- Less systemic inflammation
- Lower risk of peritonitis

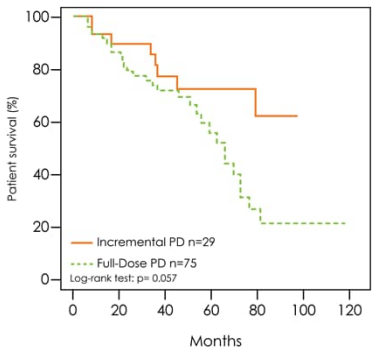
*Cox model of relative risk of death with time-dependent Ccr divided into peritoneal clearance and GFR and entered as time-dependent covariates
‡Cox model of relative risk for death with urine volume forced in as a time-dependent covariate

[1]Bargman JM, et al. *J Am Soc Nephrol*. 2001;12(10):2158-2162
[2]Chen CH, et al. *Perit Dial Int*. 2020;40(3):274-281

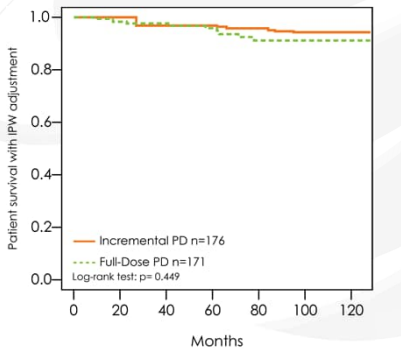
Mortality Outcomes

Incremental PD has similar patient survival to that observed with full-dose PD[1,2]

Cumulative Survival Probability in Single-Center Italian Cohort[1*]



Survival Estimate in Large, Single-Center, Korean Cohort[2‡]

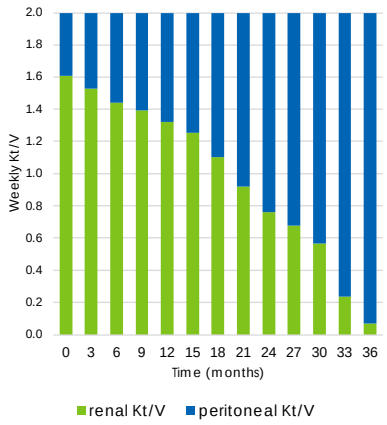


*Adapted from Figure 2 in Sandrini[1]. ‡Adapted from Figure 3 in Lee[2].

IPW: inversed probability weighted

[1]Sandrini M, et al. *J Nephrol*. 2016;29(6):871-879
[2]Lee Y, et al. *Sci Rep*. 2019;9(1)

Clinical Takeaways



- ✓ Incremental PD may be appropriate for many incident PD patients with sufficient RKF
- ✓ Patient understanding of the therapy and knowing the prescription will need to increase as RKF declines
- ✓ Appropriate clinical monitoring is essential and should consider more that Kt/V

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