

A white silhouette map of Japan is centered on a green background with a light green grid pattern. The map shows the four main islands: Hokkaido, Honshu, Shikoku, and Kyushu.

The combination therapy, PD+HD

Complementary dialysis

Hideki Kawanishi

Tsuchiya General Hospital,

Hiroshima JAPAN

2011, Beijing



Present issues of peritoneal dialysis

- Lower survival rate of longer PD (at the time of loss of residual kidney function) compared by HD
- The limited dosage to maintain middle to large solutes
- Peritoneal deterioration depended on PD vintage, and development of final complication EPS

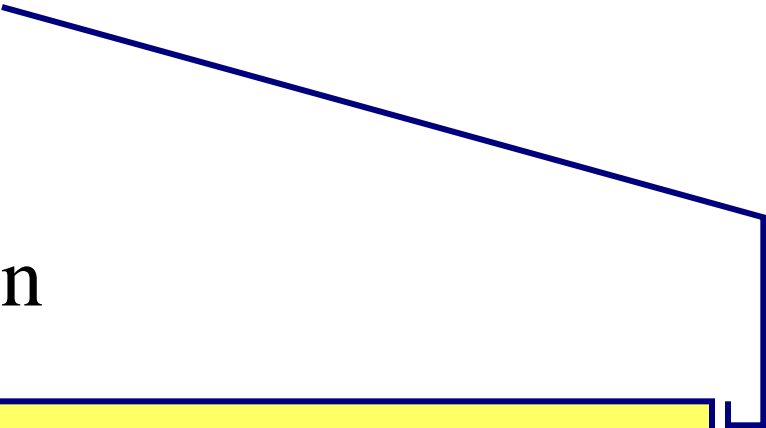
EPS (encapsulating peritoneal sclerosis)



Solutions of these PD issues

Issues

- The limited dosage
- Loss of RKF
- Peritoneal deterioration



Complementary dialysis
PD+HD used by biocompatible
PD solutions

New concept of PD


Complementary dialysis

Combination therapy PD with HD

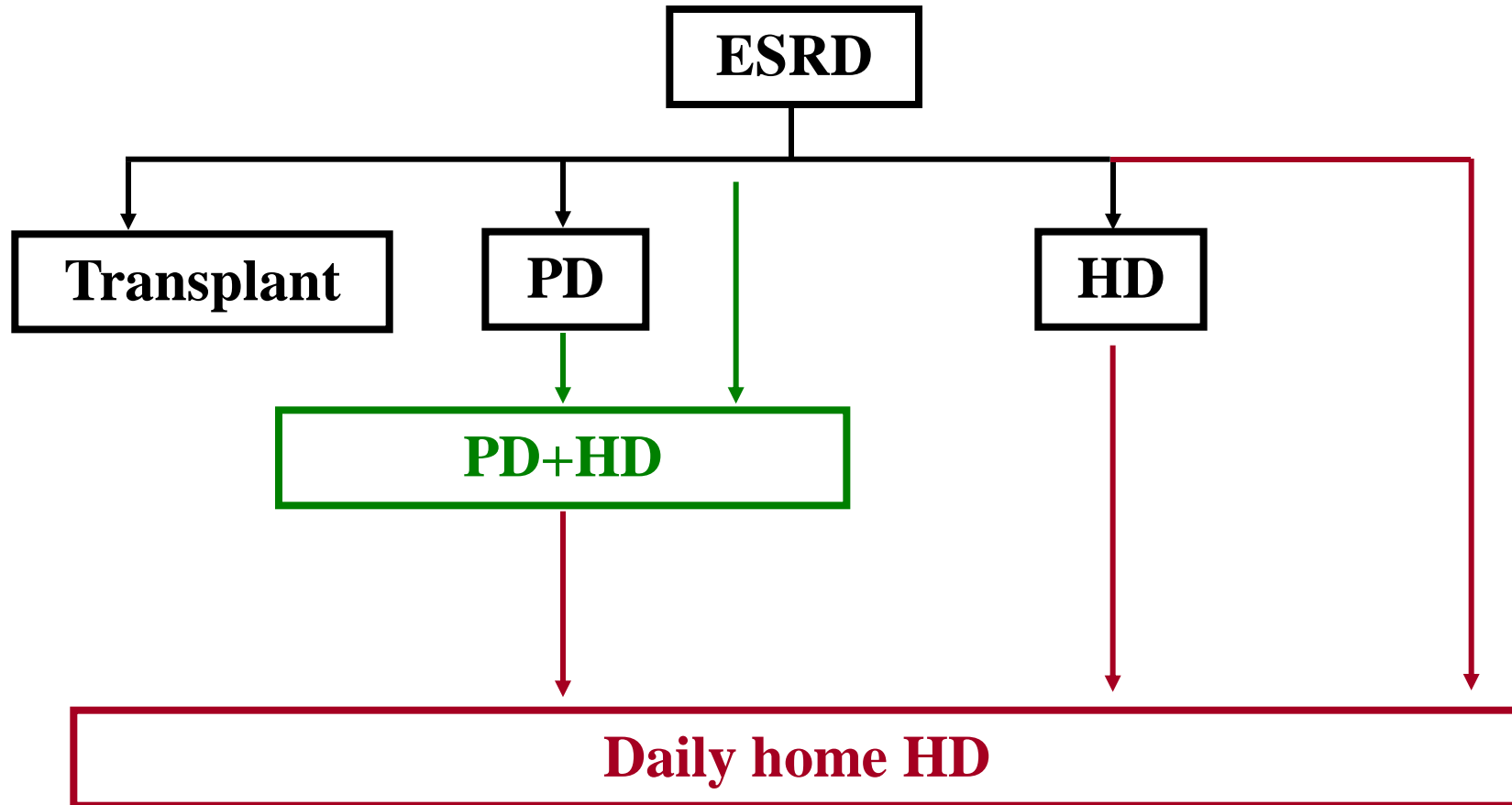
PD + RKF + HD

Concept

- The benefit of PD is the continuous nature, which results in steady-state levels of electrolytes, as well as fluid and sodium removal, and acid-base balance.
- PD is also beneficial in maintaining residual kidney function (RKF), which is known to be a determinant of survival.
- Even if successful outcome of PD in anuric patients have been reported, standard PD may, when RKF declines, not be sufficient to avoid the risk of uremic complications.
- Increasing the dose of dialysis, currently the only available diminishing these risks, indicated no benefit on survival from ADEMEX & Hong Kong studies.

- 
- An alternative to increasing the dose of dialysis in anuric patients is to combine PD with HD
 - In Japan combination therapy of weekly HD started in 1995.
 - Later, limited experiences with combination therapy have also been reported from the US and UK.

My personal selection of RRT



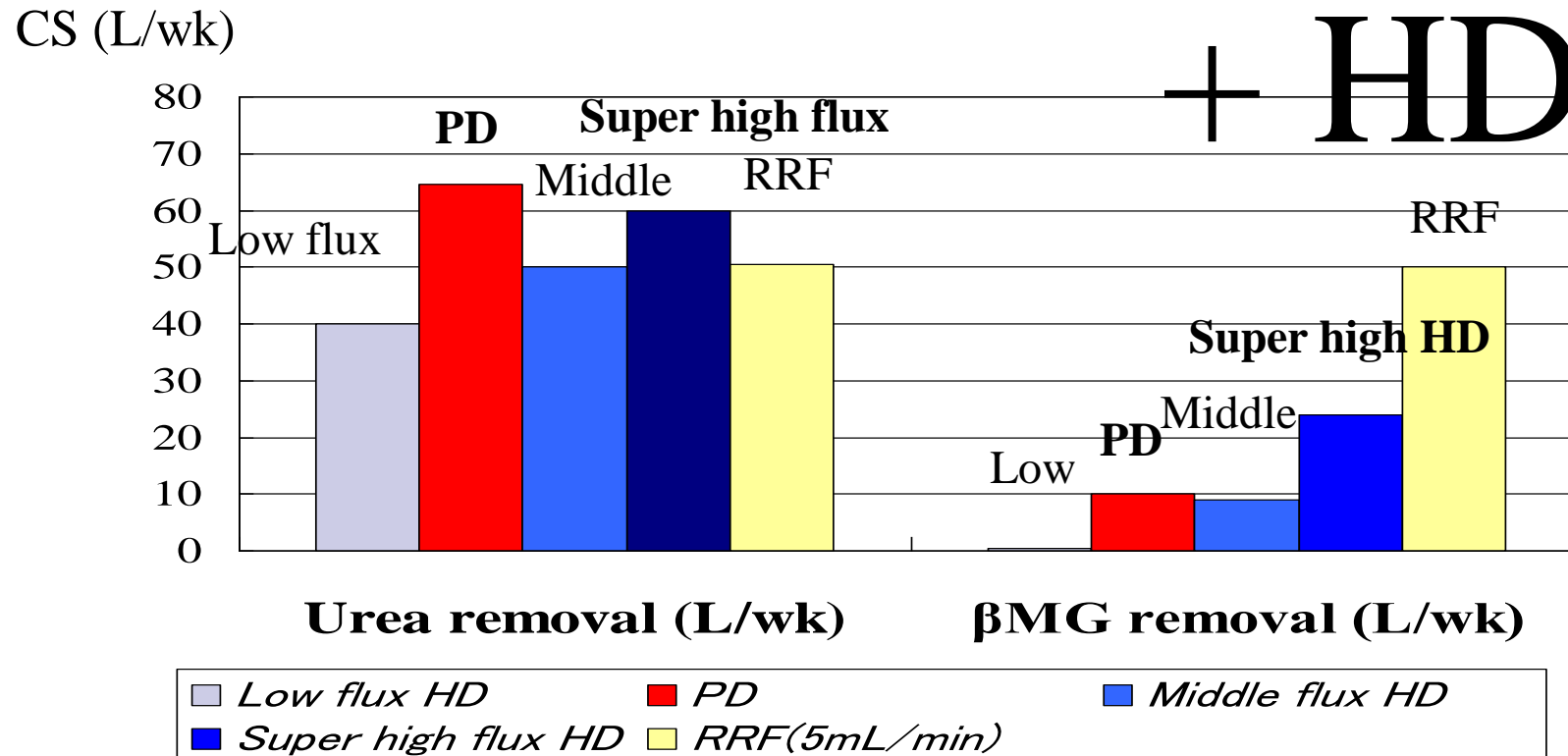
Advantage of PD

- Preservation of RKF
- Continuous dialysis: “*daily dialysis*”
 - Steady-state levels of electrolytes and acid-base balance,
 - Fluid and sodium removal,

Disadvantage of PD

Limited Removal dose of large solutes

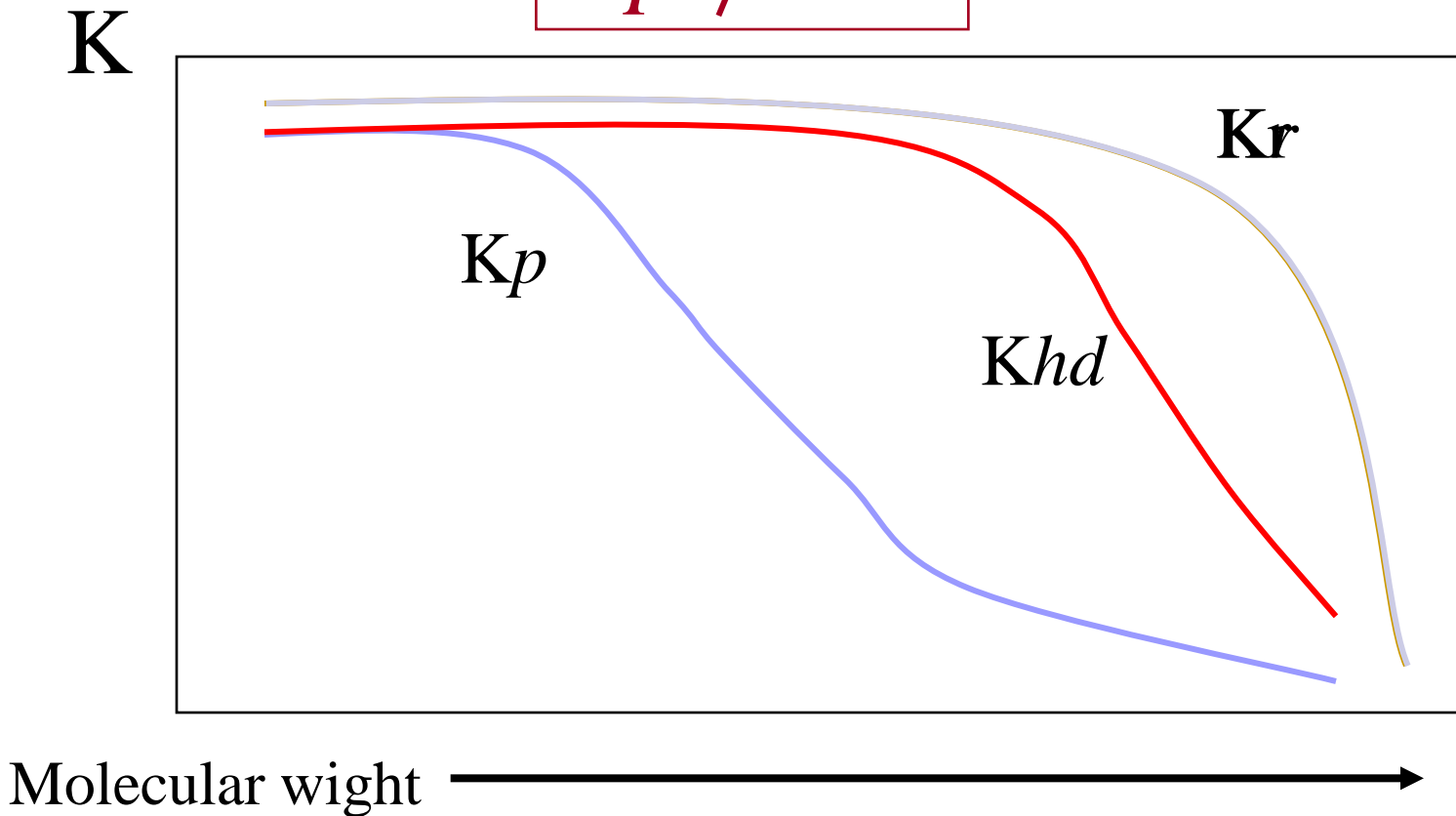
PD is one of the tool of urea removal



Clear Space= Removal volume/C(0) by Yamashita

Hypothesis of combine PD & HD;

$$K_p \neq K_r$$



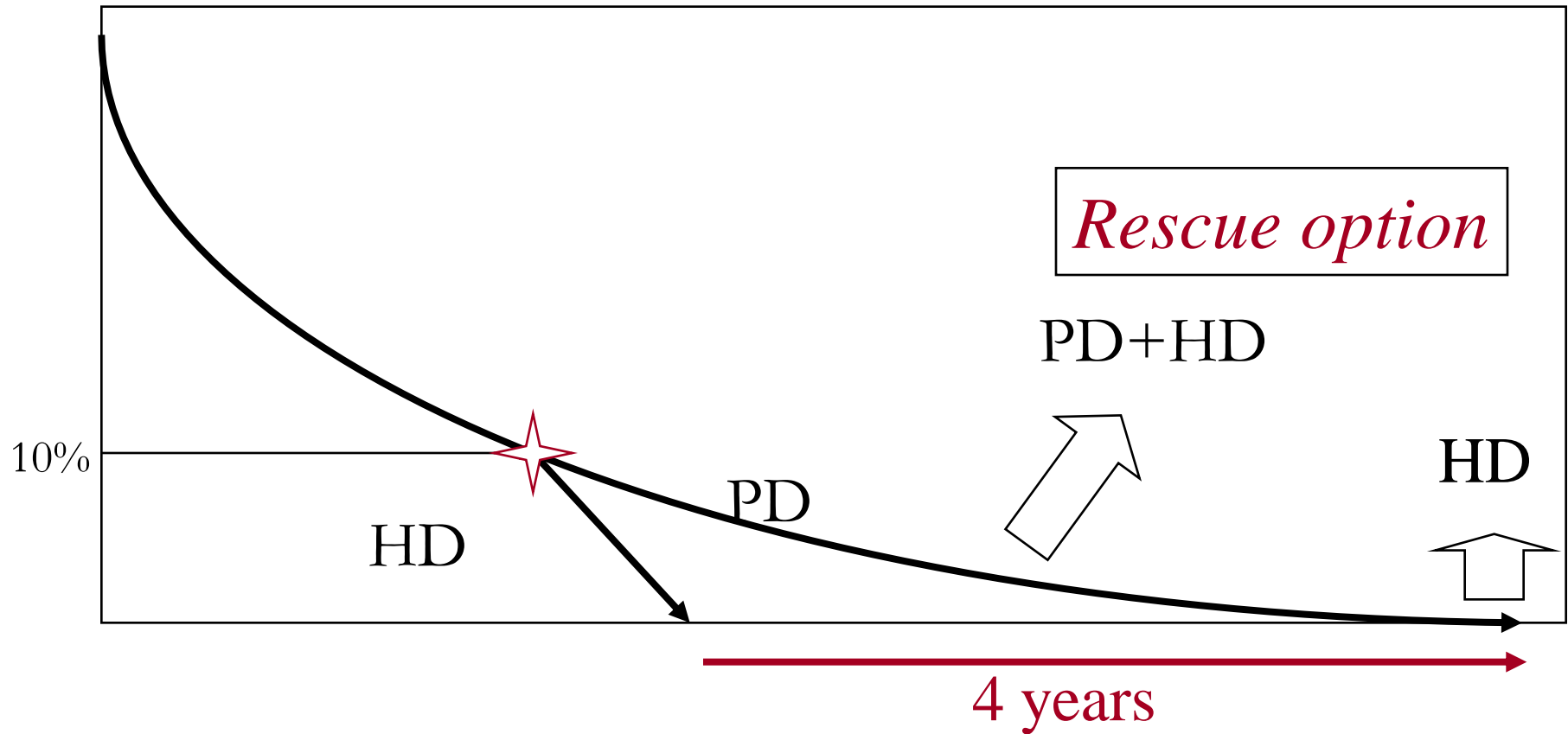
$$K_r + K_p + K_{hd} = \text{complementary dialysis}$$

Historical PD+HD combination therapy

- 1997: “PD+HD combination therapy study group, chaired by Ota K .
- 1999: Kawanishi presented “HD together with PD” and calculation of dialysis dose used by EKR in *Advance PD*
- 2003: Burkart presented US data in *PDI*
- 2003: Committee meeting of ISPD in Seattle & San Diego
 - Recommended name of “***Complementary dialysis***”
- 2004: McIntyre, Bi-modal dialysis in *PDI*

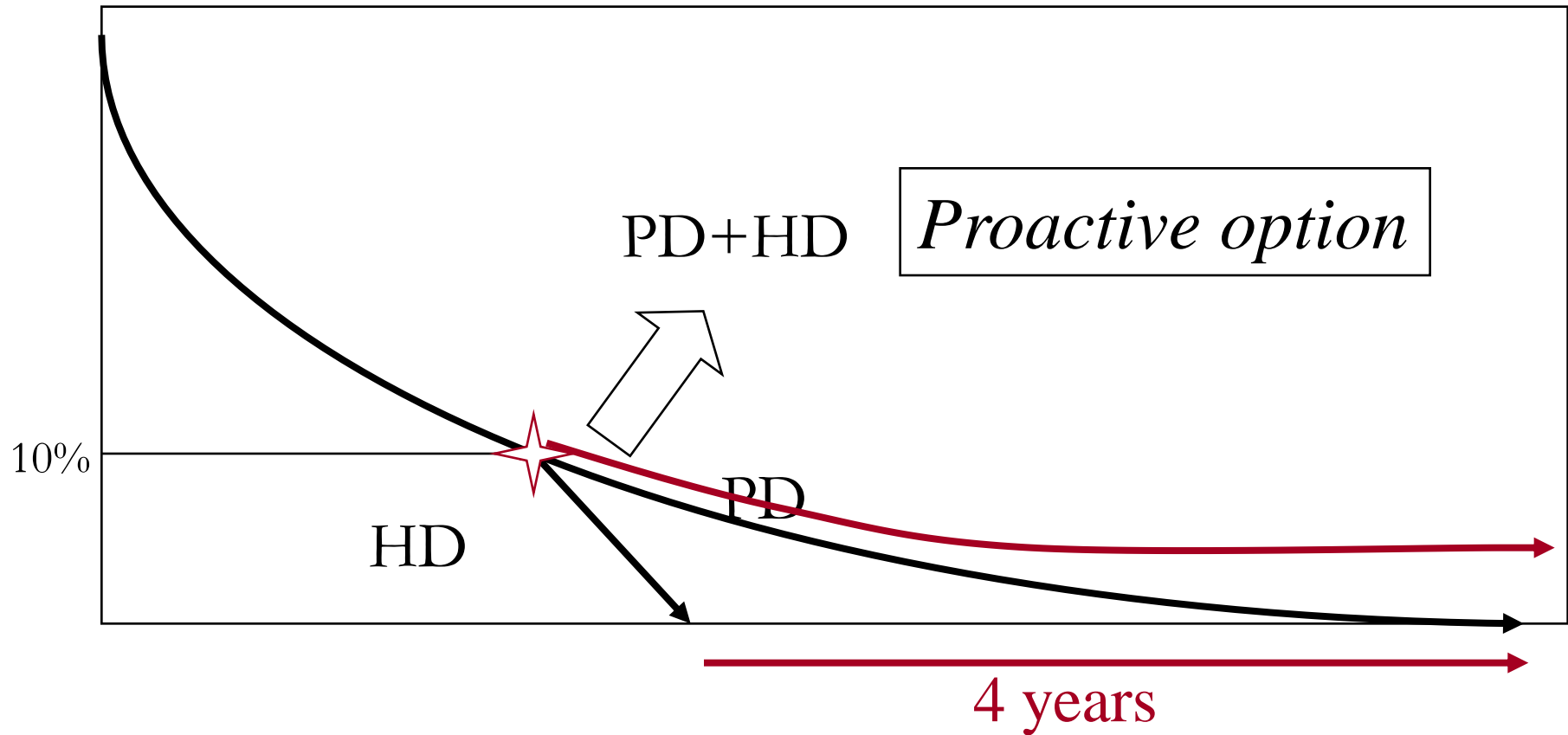
Inform to patients of PD or HD

KF



Inform to patients of PD or HD

KF



The slide features several decorative circles. At the top, there are three overlapping circles: a white one on the left, a solid light purple one in the middle, and another white one on the right. Below the main text, there are two solid light purple circles on the left and one white circle on the right. The text 'General indications for combination therapy PD & HD' is centered across the top circles, and 'Rescue option' is centered across the bottom circles.

General indications for combination therapy PD & HD

Rescue option

Potential indications for combine PD & HD

Kawanishi H PDI 2006, 26

- Patients, in which PD dose increase not compatible with patient's life style or subjective tolerance of increased fill volume, with
 - *Insufficient small solute clearance resulting in*
 - uremic symptoms,
 - excessive potassium/ sodium/ phosphate and/ or protein intake.
 - *Fluid over load*
 - ultrafiltration failure,
 - difficult to manage fluid balance because of poor self-management,
 - severe heart failure

Potential indications for combine PD & HD.

- Medical reasons for not increasing PD solution, e.g. limited peritoneal capacity, hernia, hydrothorax
- Severe mental stress due to PD; *PD holiday*
- Peritoneal rest (with expectation of improved peritoneal function of membrane deterioration)
- HD patients with cardiovascular instability

KT/V

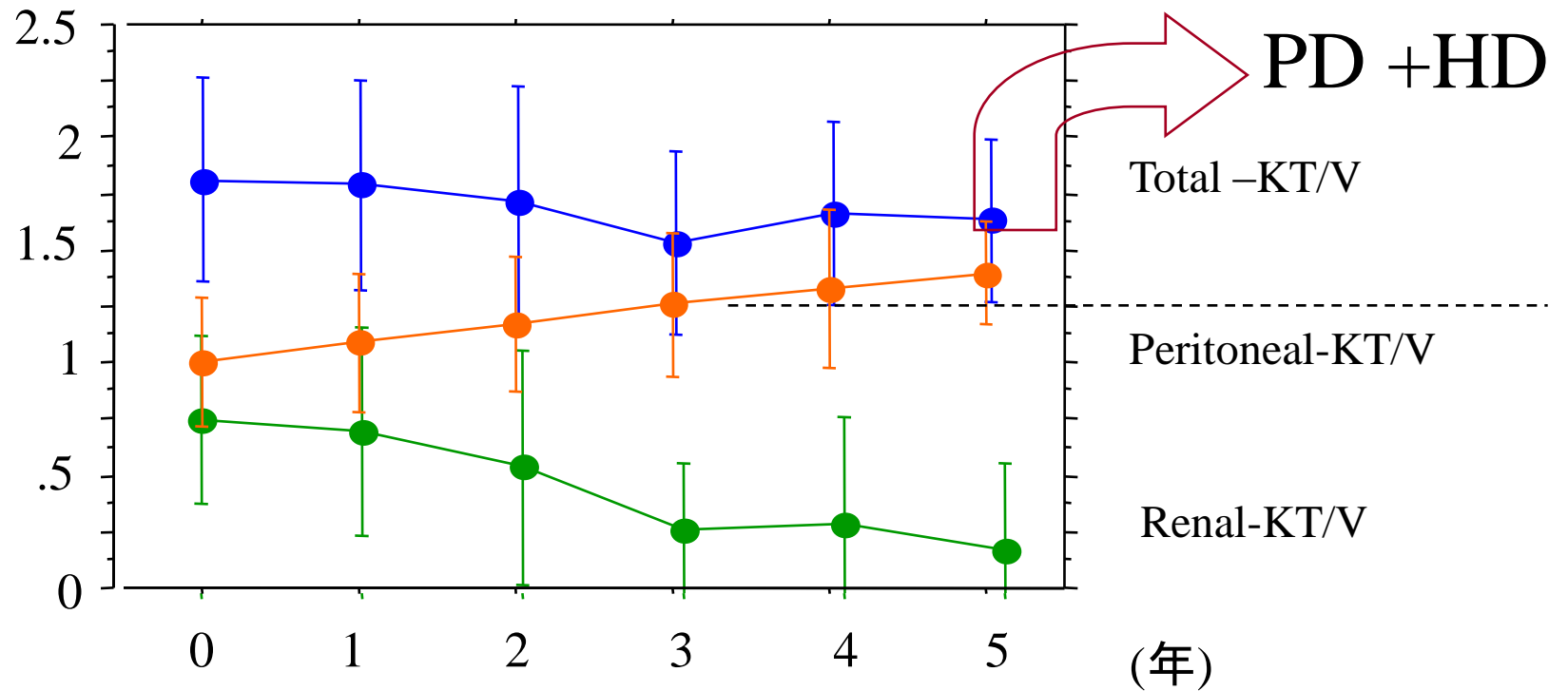
PD: 66 cases, PD vintage > 24 months

Age: 60.6 ± 11.0

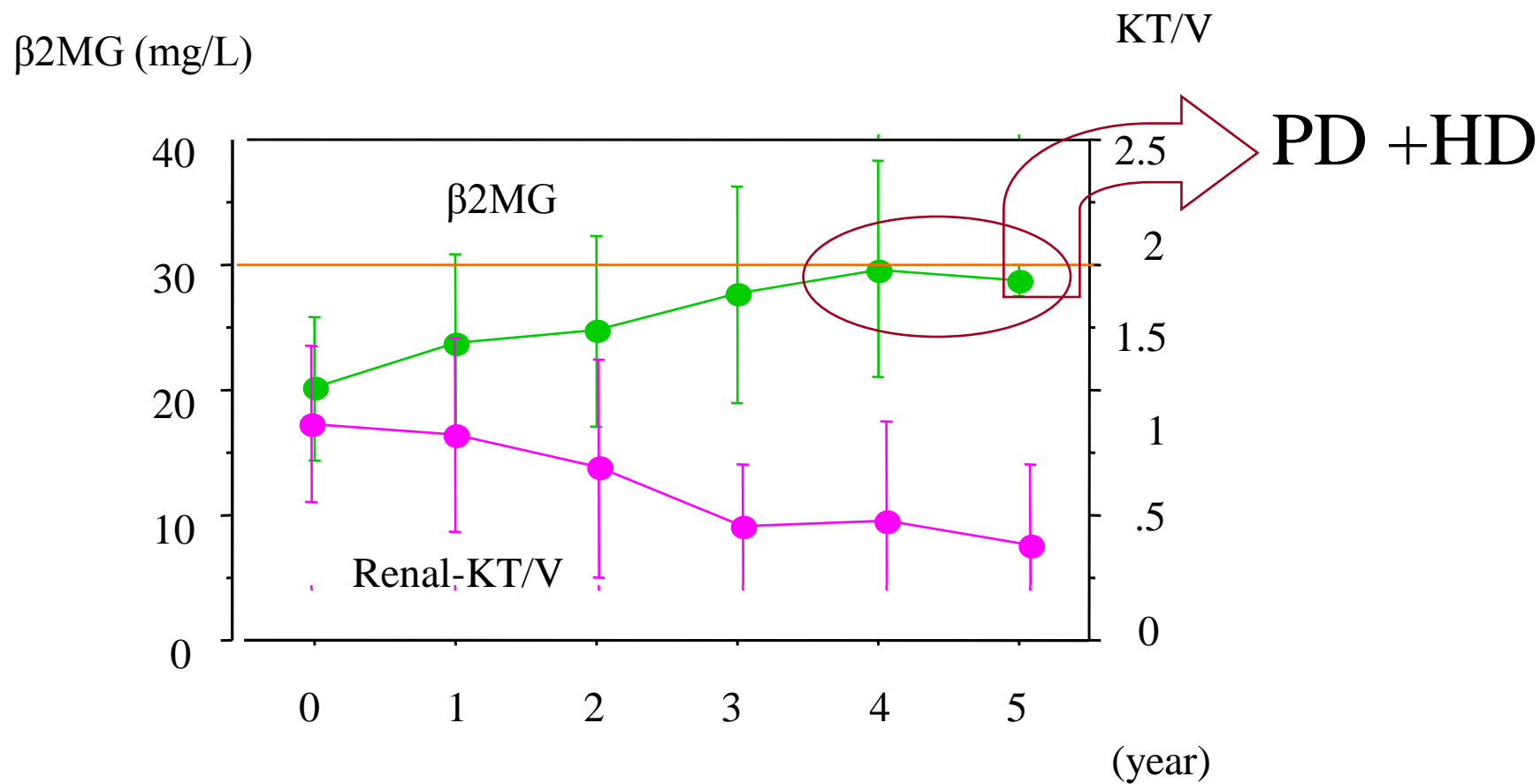
DM/non-DM 6/60

Gender M/F 44/22

KT/V

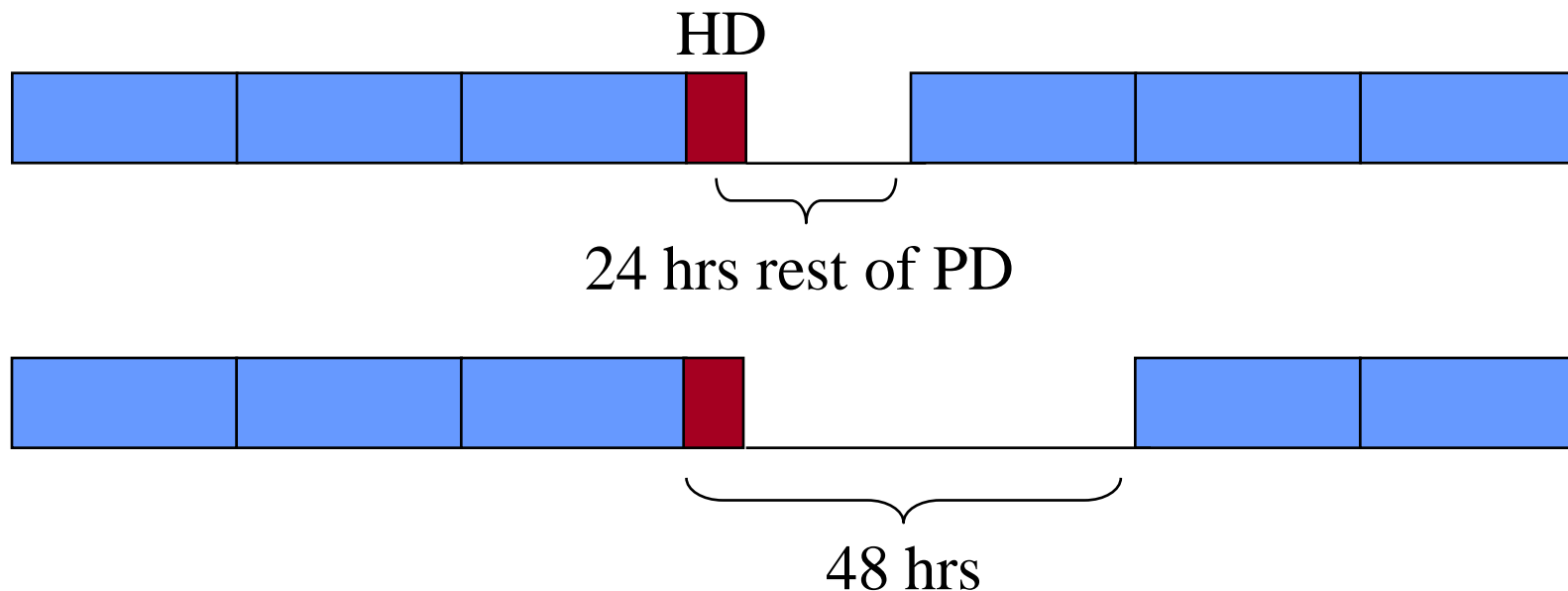


β 2MG



Common prescription of combine PD & HD in Japan

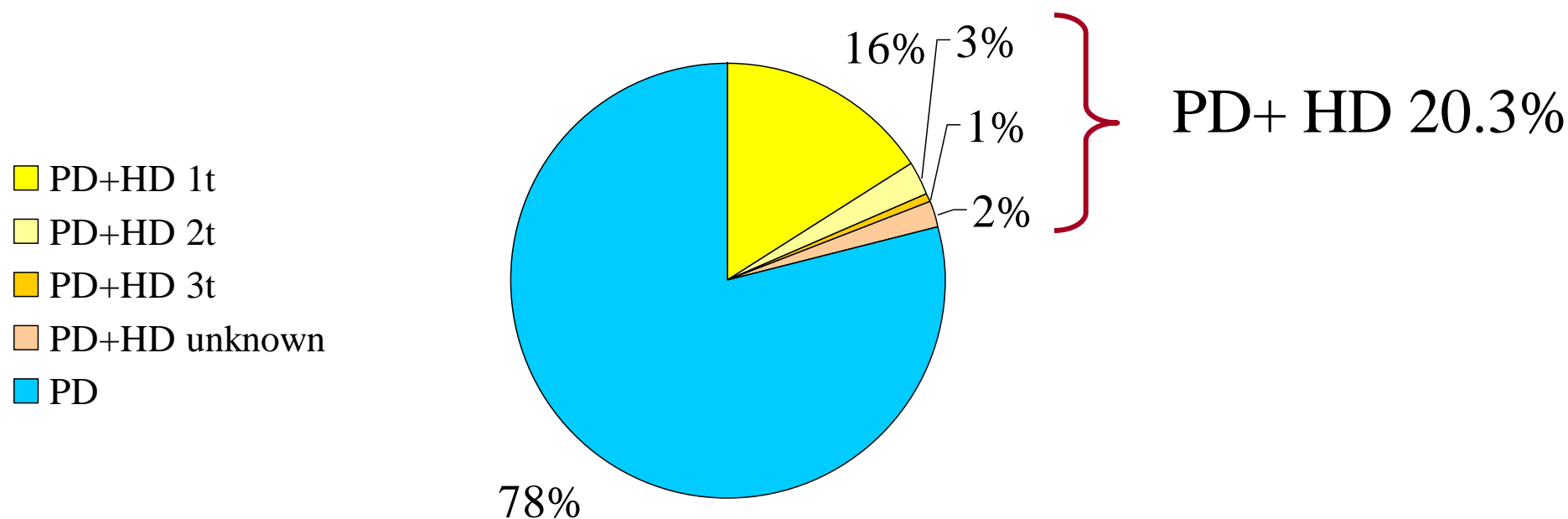
- Six or Five days PD,
and 1 times *4hrs*-HD used super highflux membrane



Number of patients combine PD & HD in Japan

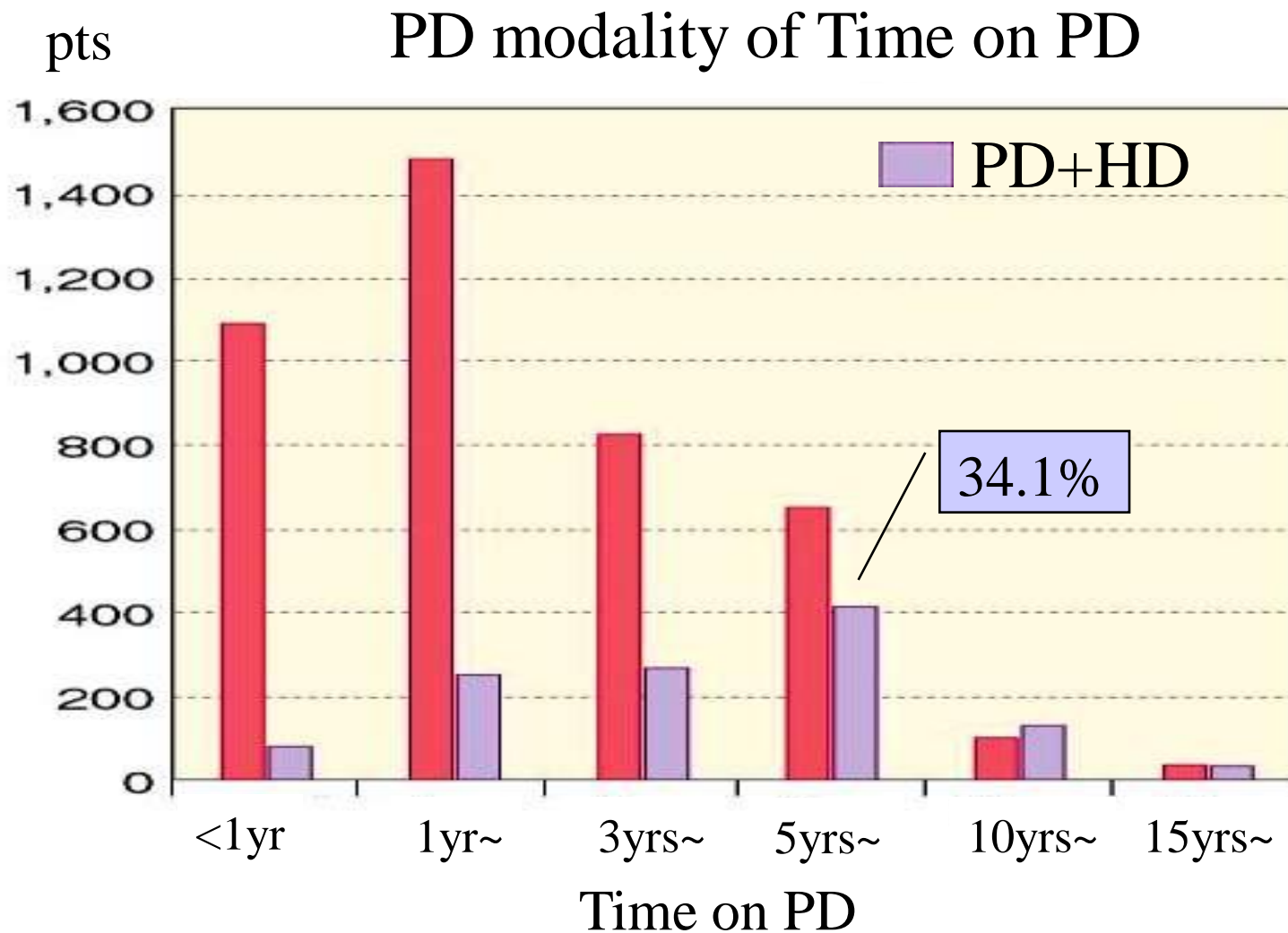
JSDT end of 2010

- Dialysis pts: 297,126
- PD pts: 9,728 (3.3%)

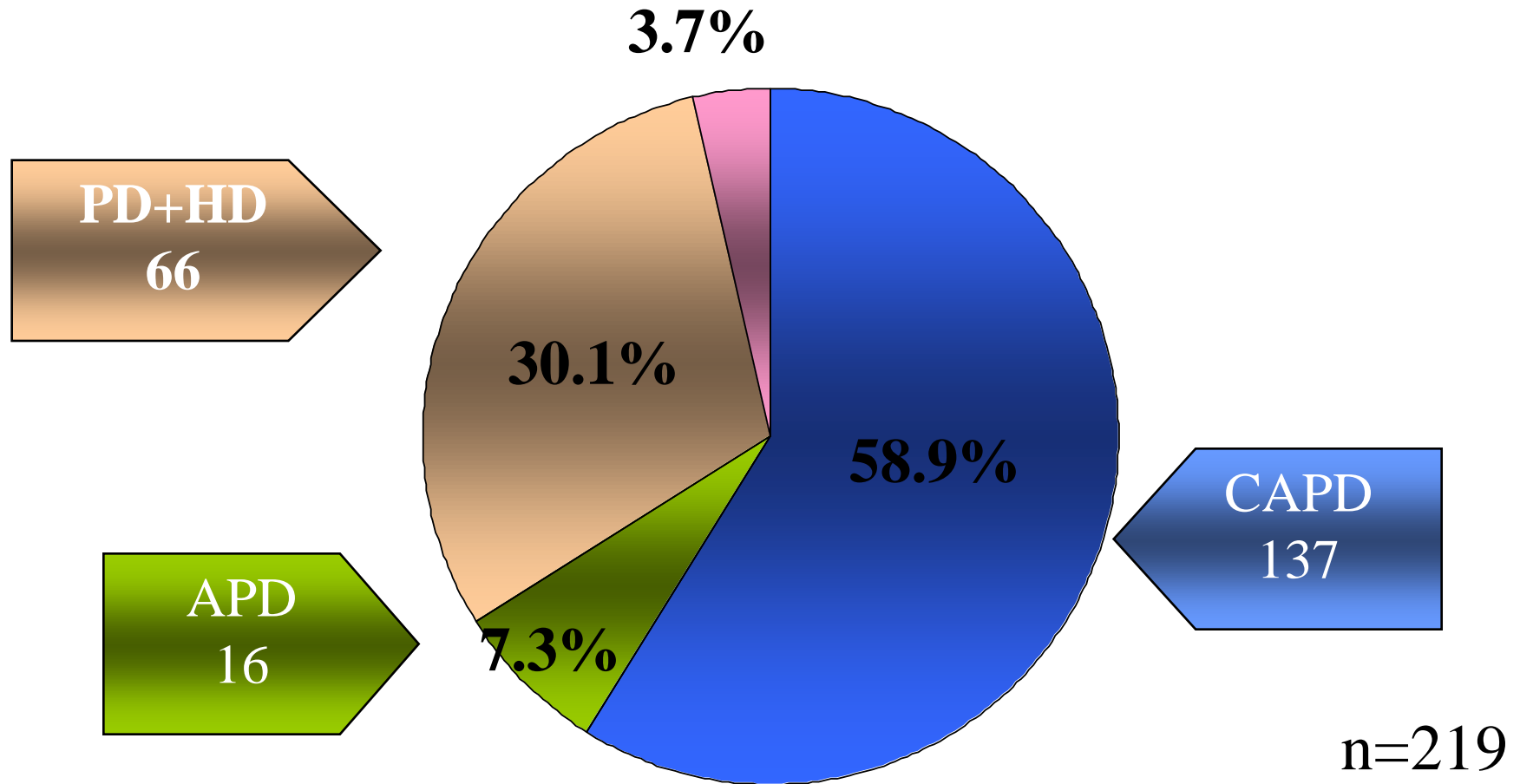


Number of patients combine PD & HD in Japan

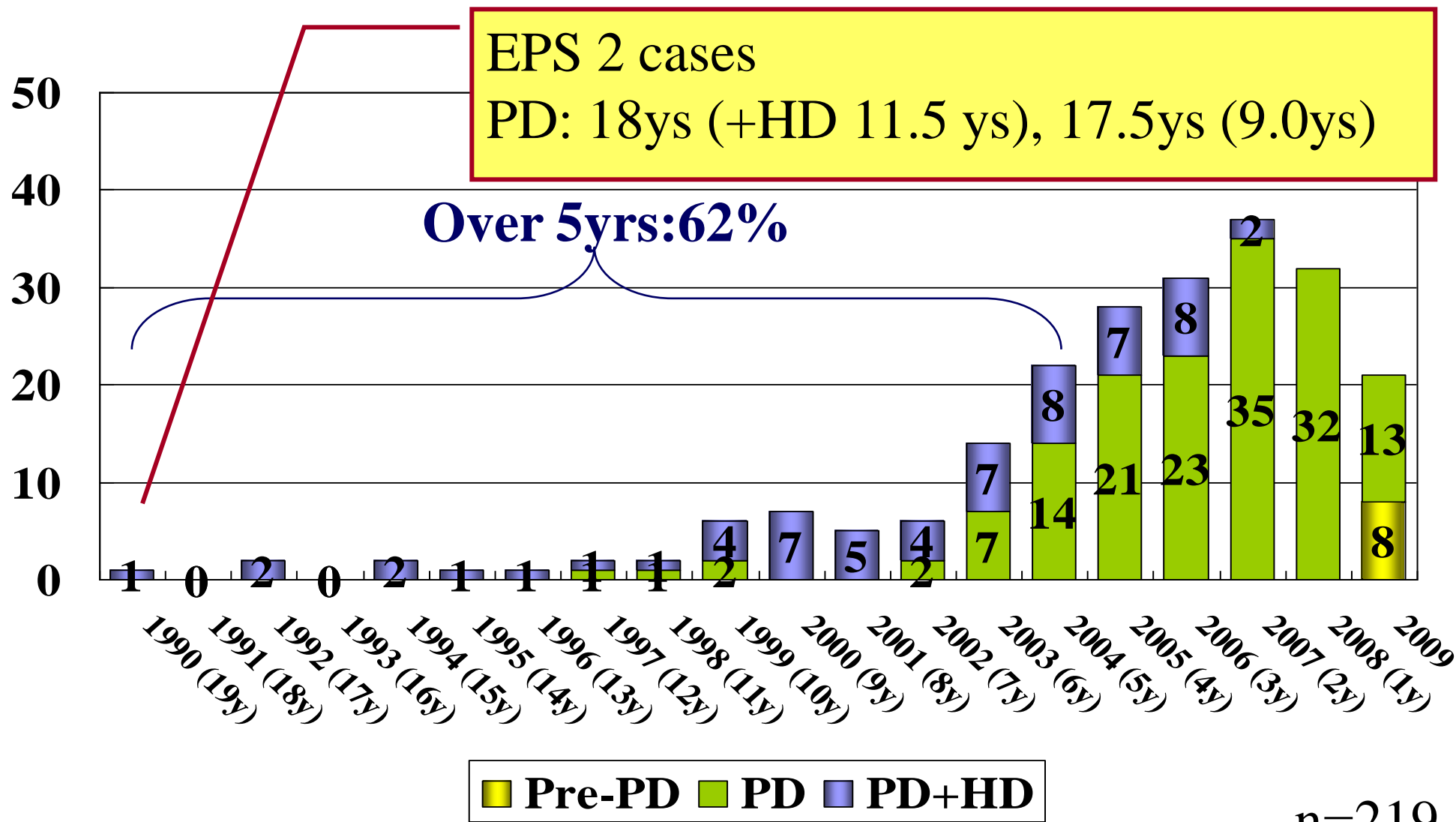
JSDT end of 2009



Modality of PD in Tsuchiya General Hospital



PD vintage in Tsuchiya General Hospital



n=219

Evaluation of dialysis dose during combine PD & HD

- Equivalent renal urea clearance (EKR) by *Kawanishi H, Adv PD 1999*
 - Calculation of HD dose ($EKR = G / TAC$) + PD dose
- Urea reduction rate (URR) by *Vonesh E, ASN2004*
- Fractional solute removal (FSR) by *Debowska M & Lindholm B, ASIO J 2007*
- Total effluent sampling of PD and HD : Clear Space by *Yamashita A*
 - PD: weekly total effluent volume x D/P
 - HD: effluent volume per HD x (Effluent/plasma (C0) ratio)

Equivalent renal urea clearance (EKR)

- Extraction urea dose of HD

$$\text{EKR}(\text{equivalent renal urea clearance, ml/min}) = G/\text{TAC}$$

(G; urea generation rate, TAC; time-averaged concentration of urea)

$$\text{TAC} = \{[\text{td} \times (\text{CO1} + \text{Ct})] + [\text{tid} \times (\text{Ct} + \text{CO2})]\} / 2 (\text{td} + \text{tid})$$

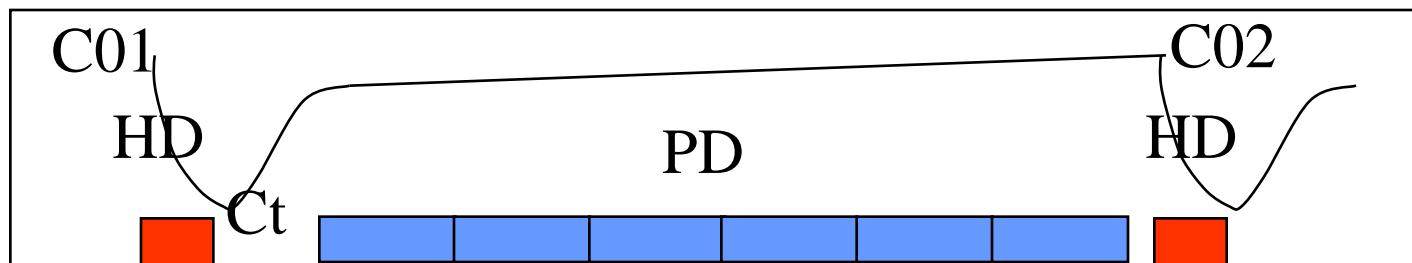
$$G = V \times (\text{CO2} - \text{Ct}) \times 10 / \text{tid}$$

Td: hemodialysis session length (min), tid: inter-hemodialysis time (min)

CO1, CO2, Ct : blood concentration pre and post dialysis

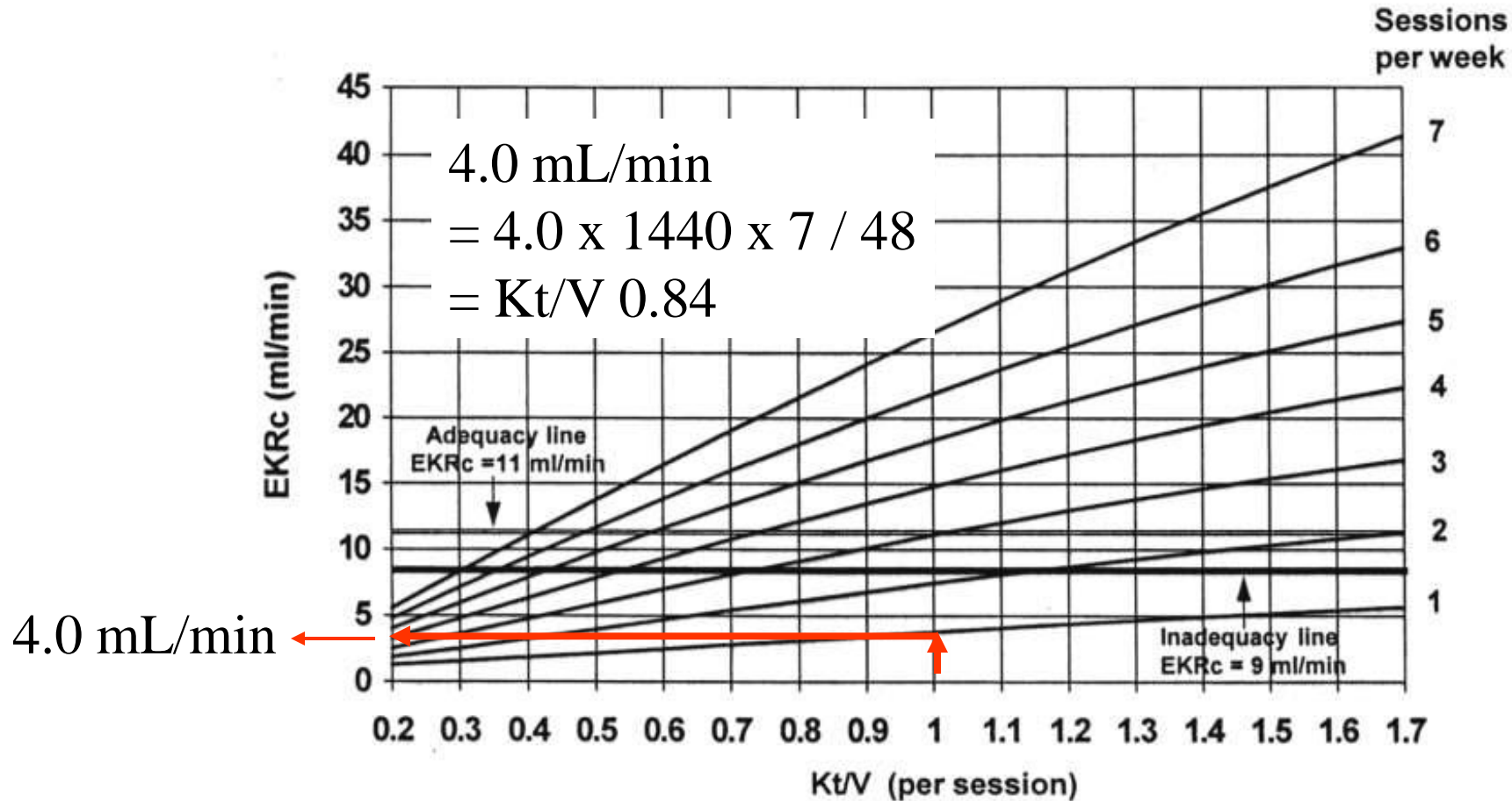
- Calculation for PD dose

$$\text{Kp ml/min} = \{ \text{urea D/P} \times \text{total effluent volume(ml)} / 24(\text{hr}) \times 60(\text{min}) \}$$



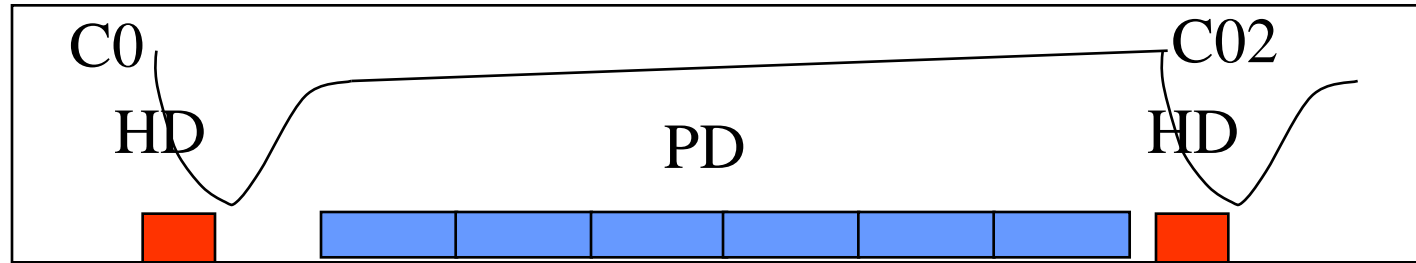
EKR: equivalent renal urea clearance

$$EKR = G / TAC$$



Total effluent sampling of PD and HD (Clear Space)

Kawanishi H et al., Adv PD 2007



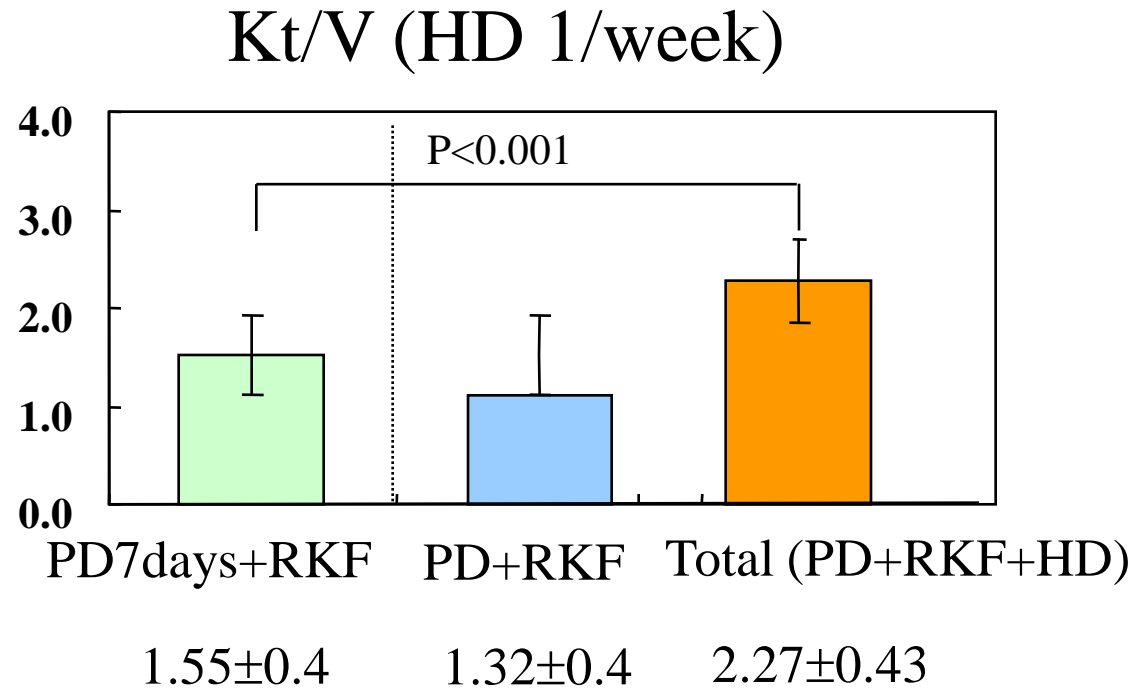
HD dose: Effluent volume per HD \times Effluent/plasma (C0) solute co

PD dose: Daily effluent volume per PD \times D/P \times weekly PD days

- Kt/V -CS, C_{cr} -CS
- V, BSA: post hemodialysis,
- V: Watson's, BSA: DuBois & DuBois's formula

Change of Kt/V on PD+HD

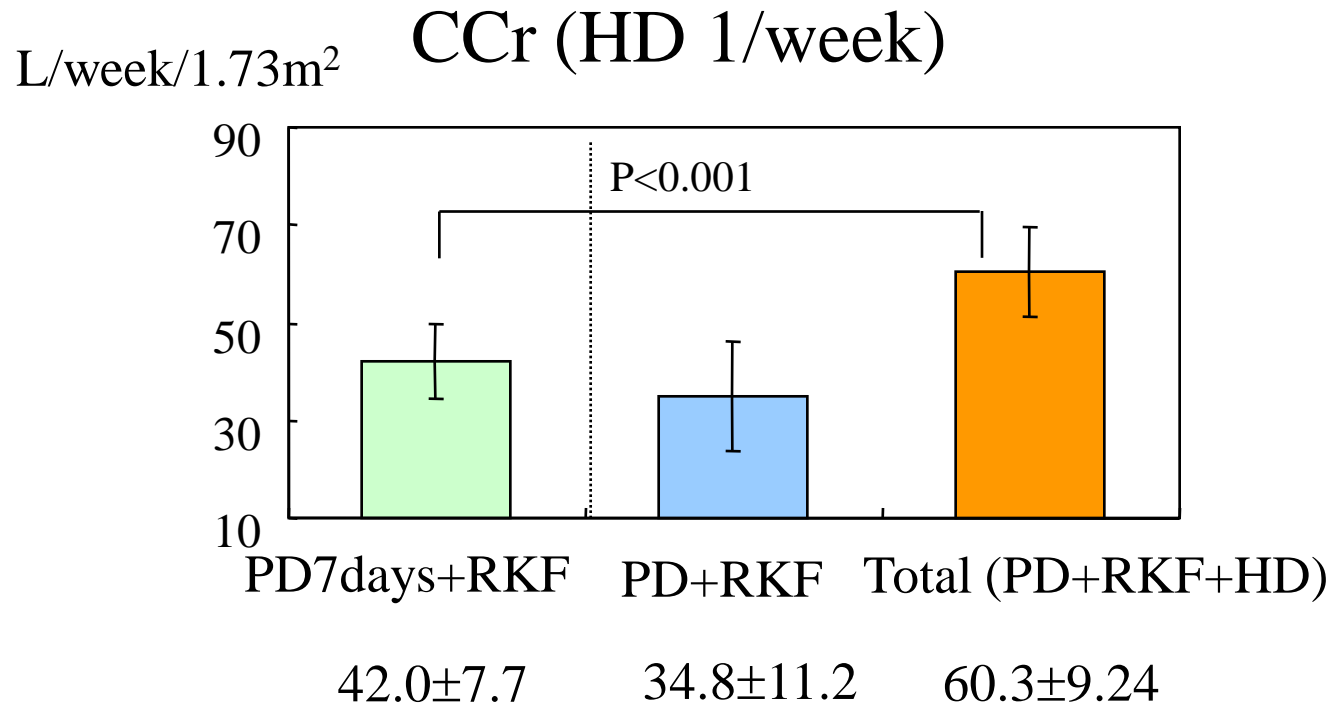
Kawanishi H et al., Adv PD 2007



Change of CCr on PD+HD

Kawanishi H et al., Adv PD 2007

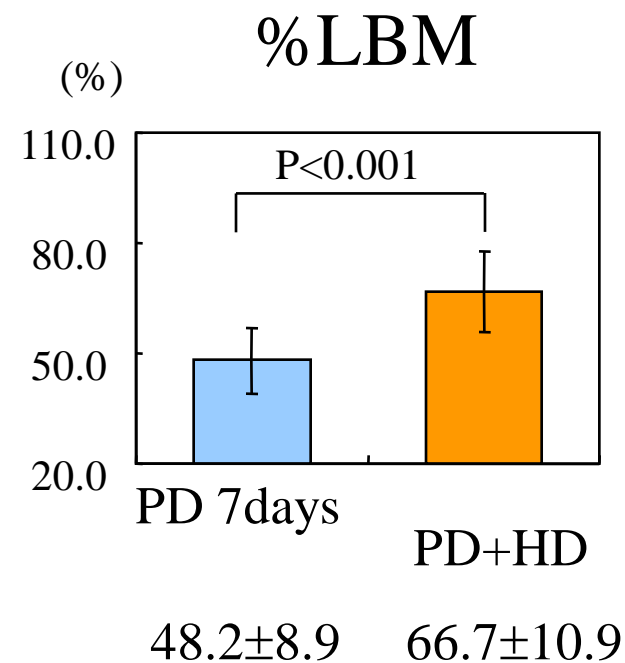
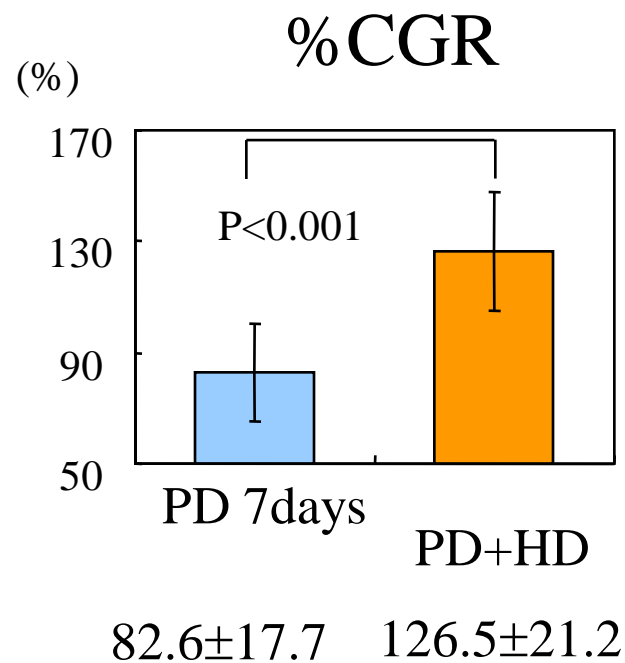
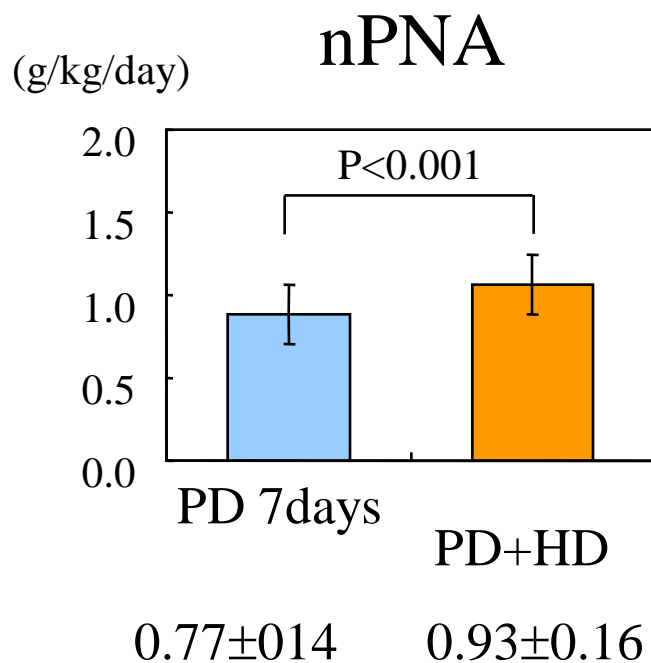
Clinical effects



nPNA, %CGR, %LBM

Kawanishi H et al., Adv PD 2007

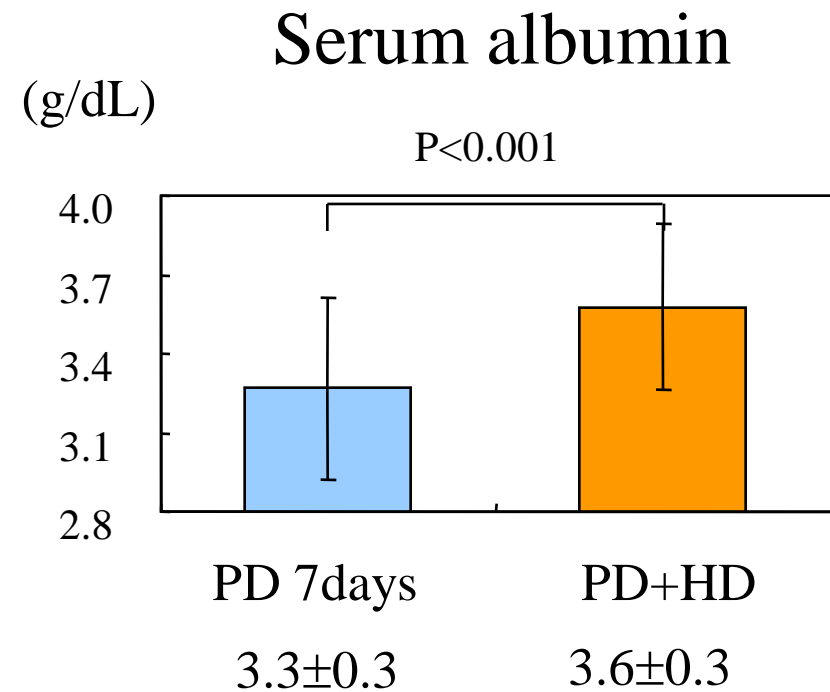
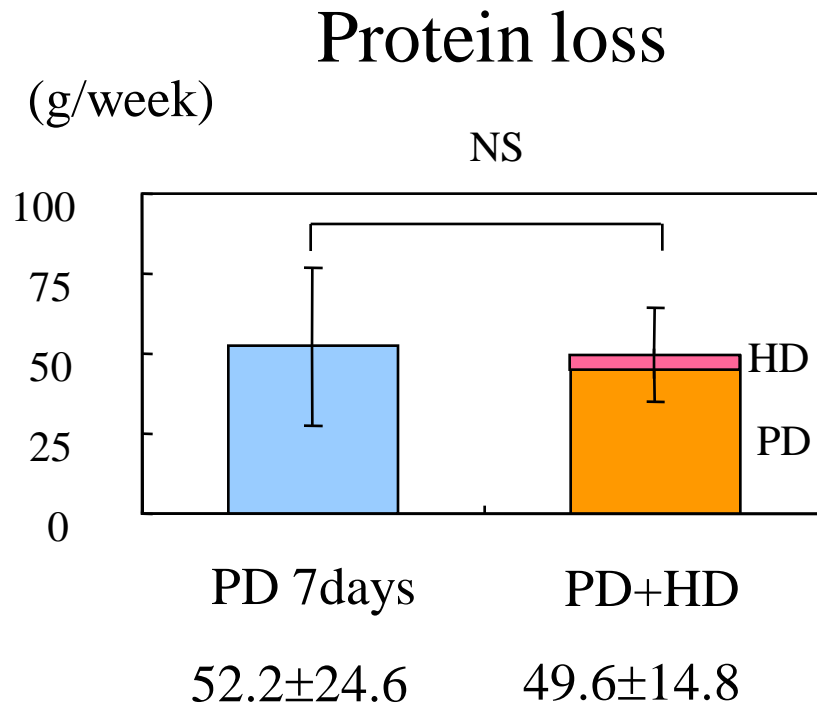
Clinical effects



Clinical effects

Protein loss & serum albumin

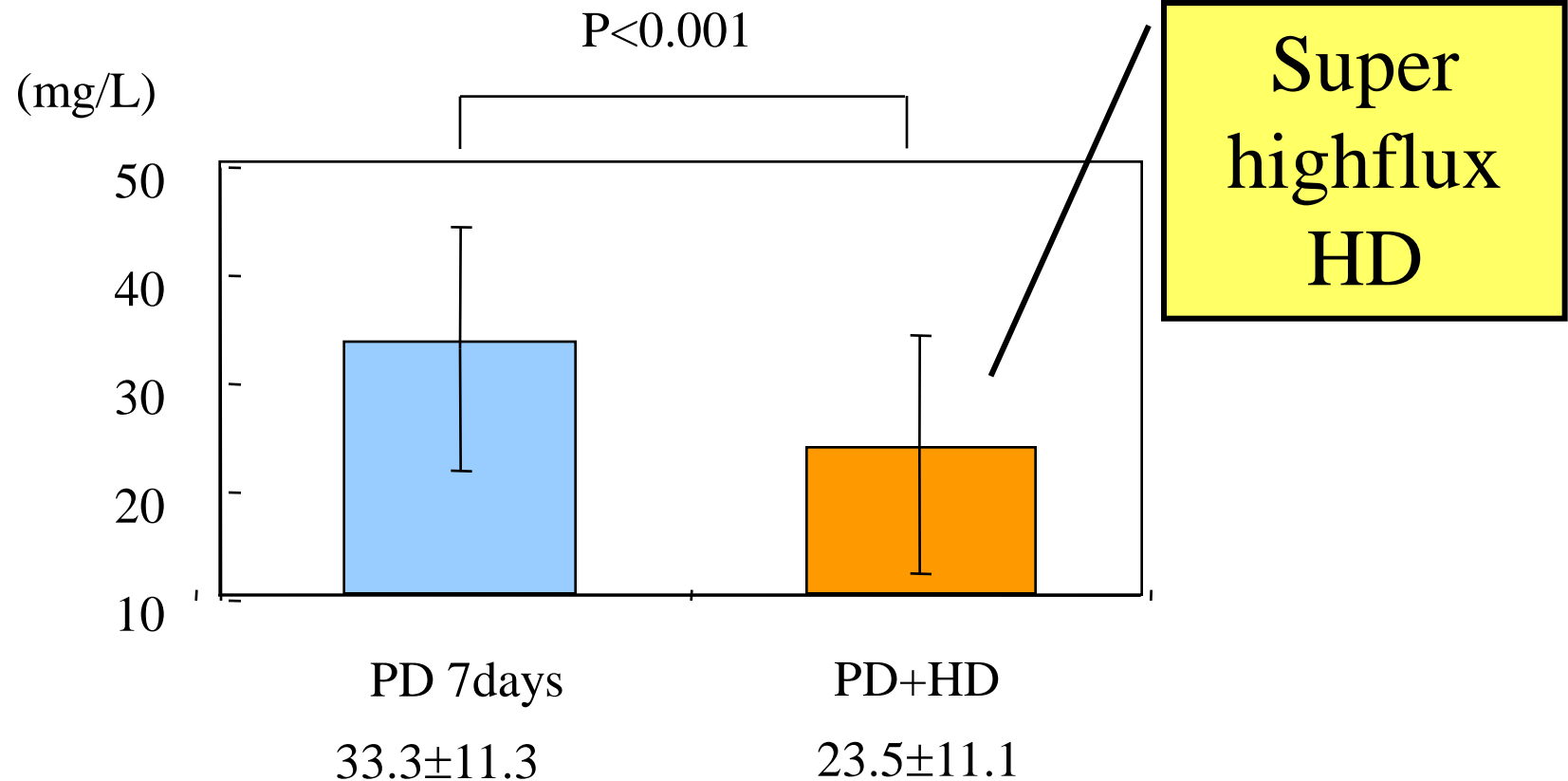
Kawanishi H et al., Adv PD 2007



Serum β_2 MG

Kawanishi H et al., Adv PD 2007

Clinical effects



Tsuchiya General Hospital



Question ? to

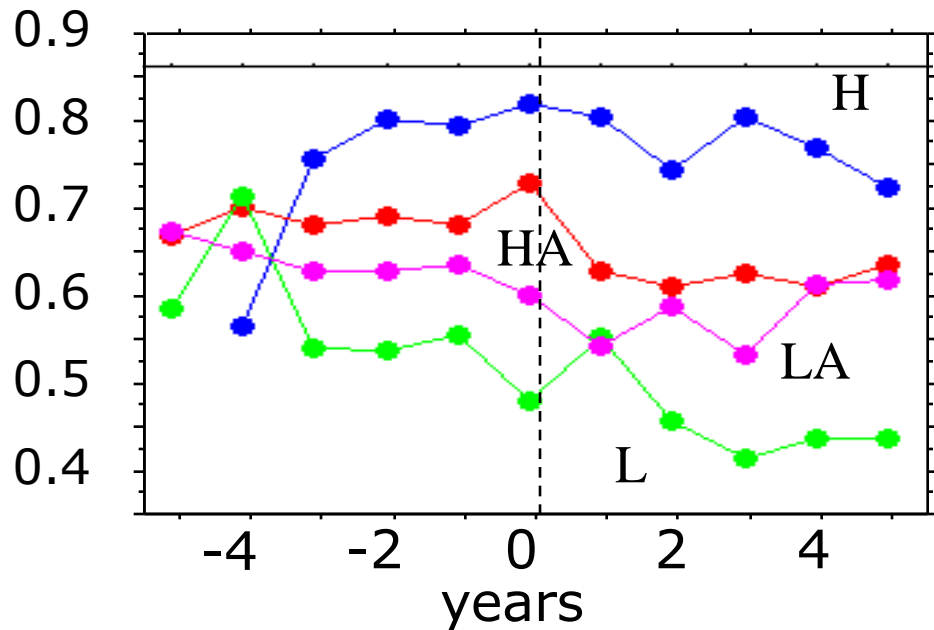


Possibility of preservation of peritoneal
deterioration on combination therapy

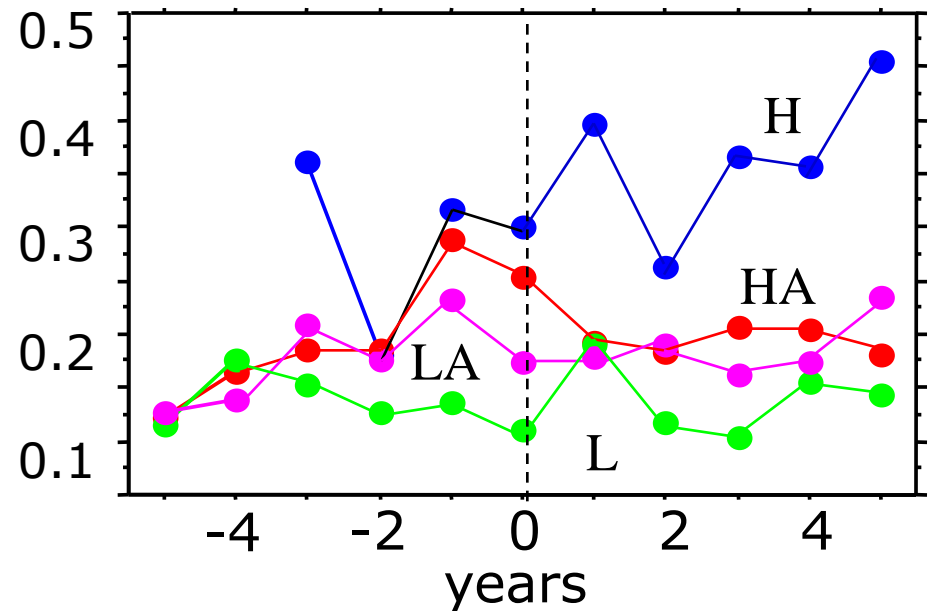
Evaluation of Peritoneal Permeability during combination Therapy with PD and HD,

Moriishi M, Kawanishi H Adv PD 2010

D/P-Cr on PET



D/P- β 2M in overnight

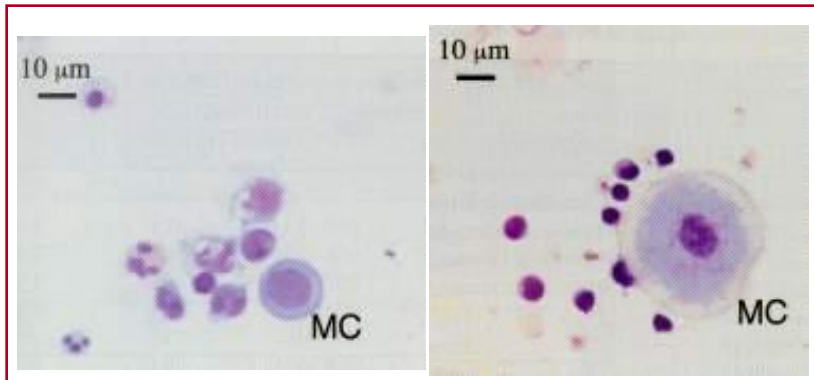


- H
- HA
- LA
- L

Mesothelial Cell Area

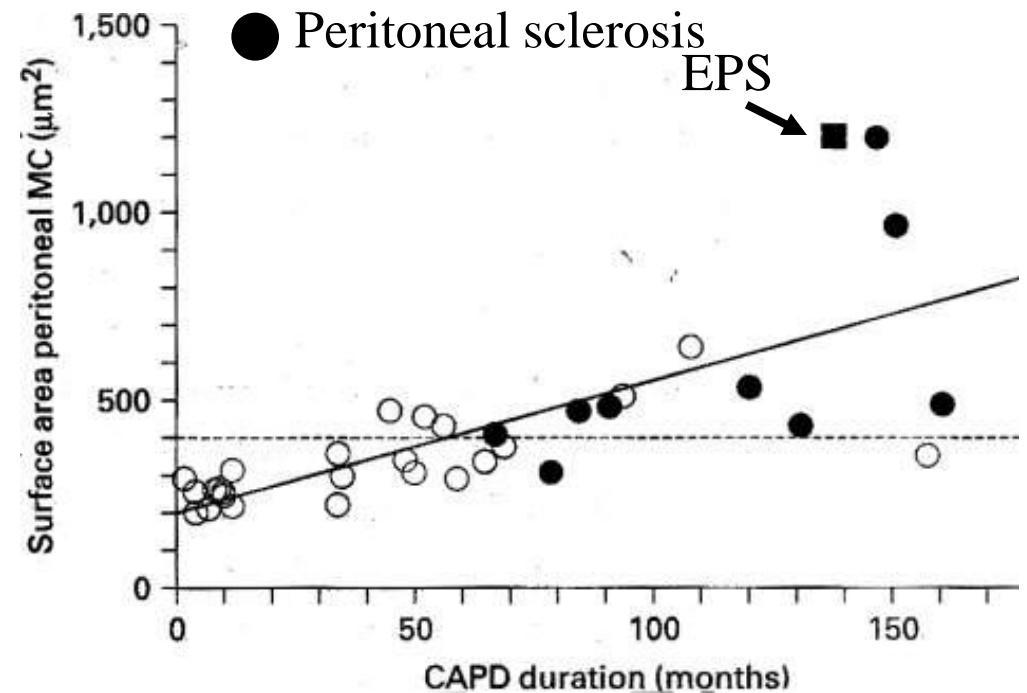
Yamamoto T et al., AJKD 1997, Izumotani T et al., Nephron 2001

- Risk of peritoneal sclerosis: Giant MC $>350\mu\text{m}^2$



Normal MC

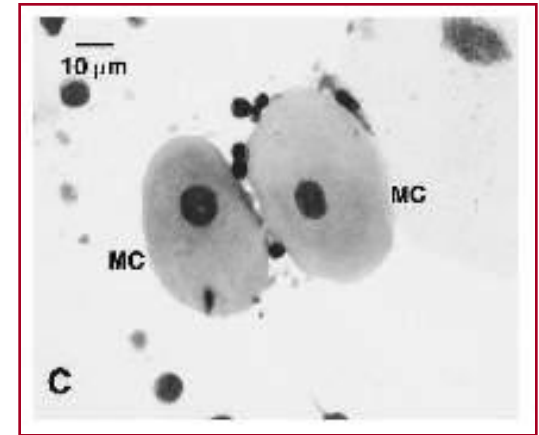
Giant MC



Effect of PD+HD to Mesothelial cell area

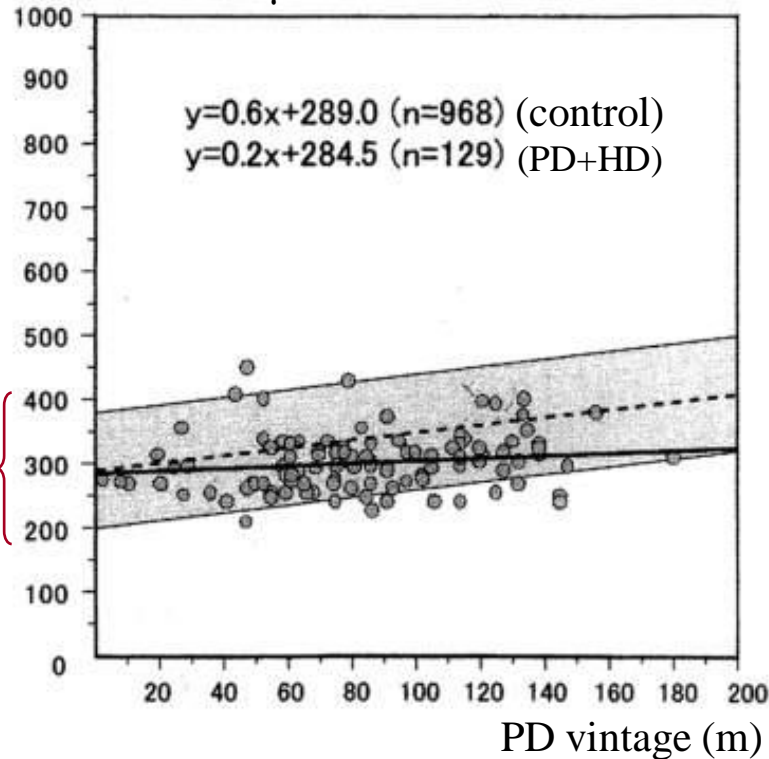
Yamamoto T et al., Jin to Touseki 2003

- PD+HD 74
- PD vintage 81.2 m (3-180), PD+HD 21.7m (1-11)
- Control (PD) 601

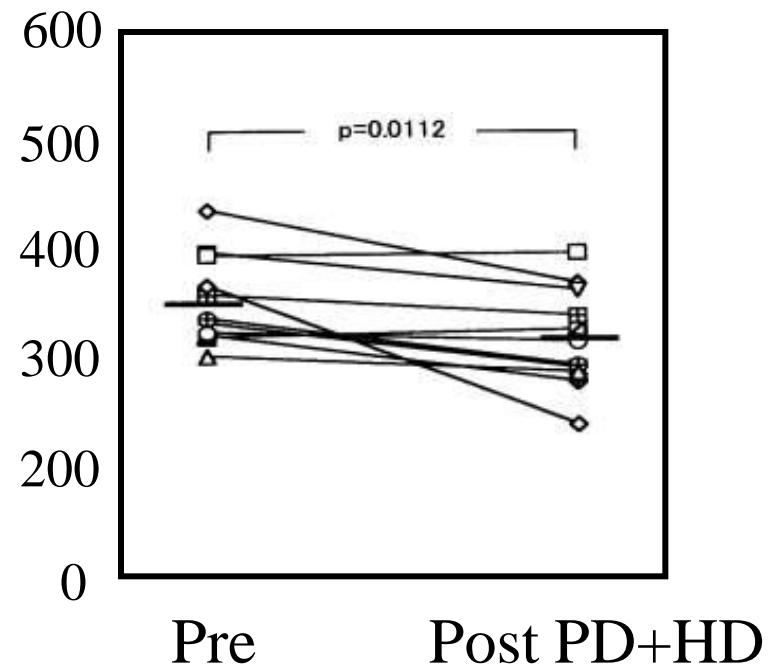


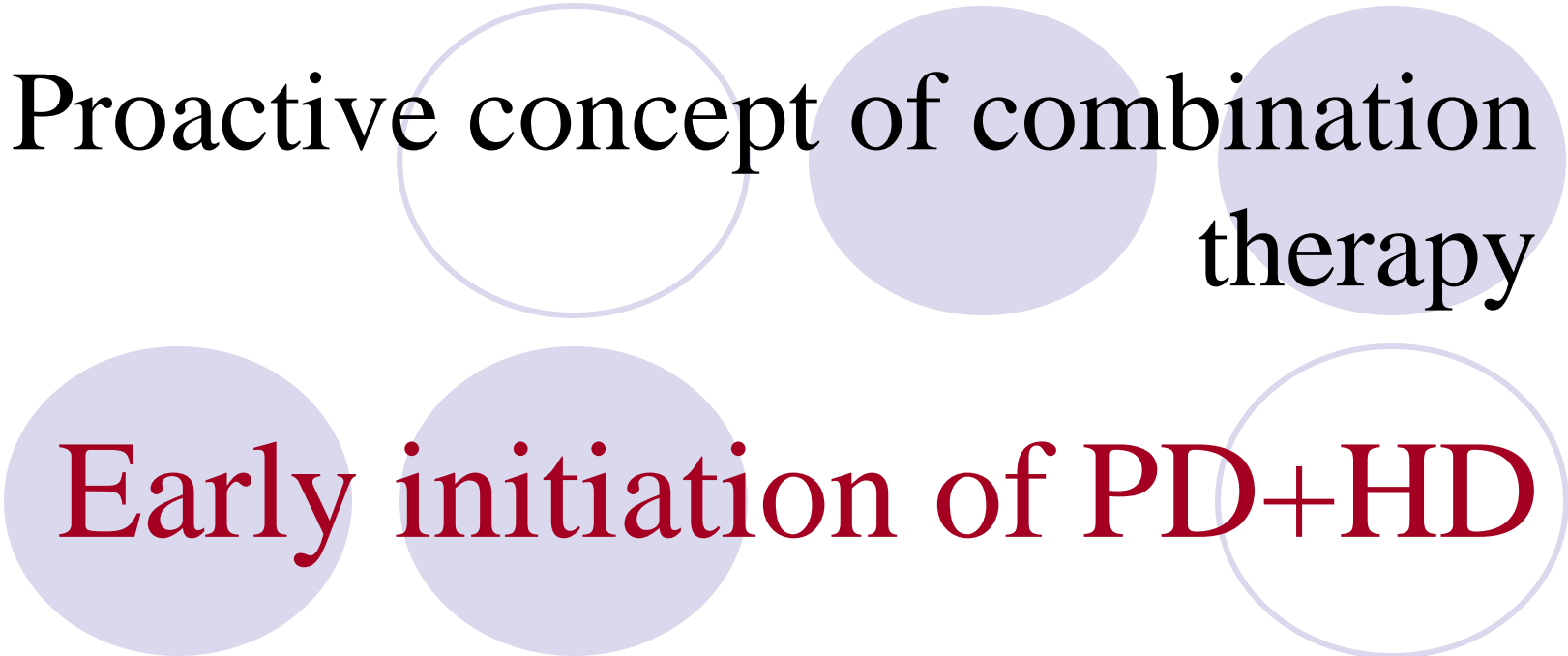
Giant MC, AJKD 1997

Mesothelial cell area μm^2



Mesothelial cell area μm^2





Proactive concept of combination
therapy

Early initiation of PD+HD

Proactive concept for complementally dialysis

- Bi-model dialysis by *McIntyre, PDI 2004*
- Early initiation of PD+HD
- Preservation of RKF
 - Dialysis dose: HD,
 - Continuous UF: PD

Dialysis Adequacy [Individual Delivered Hemodialysis (HD) Kt/V (Value Is per HD Treatment), and Weekly Peritoneal Dialysis (PD) Kt/V], Ultrafiltration Volume, and Residual Renal Function (as Measured by Chromium EDTA Clearance) Changes over the Study Period

	Initial	At 6 months	At 12 months
Kt/V HD	1.5±0.24 (1.2–1.8)	1.45±0.22 (1.1–1.8)	1.5±0.14 (1.3–1.7)
Weekly Kt/V PD	1.0±0.13 (0.8–1.1)	0.95±0.14 (0.8–1.1)	1.0±0.14 (0.8–1.2)
Chromium EDTA clearance (L/1.73 m ²)	13.6±3.4 (8–16)		12.4±2.0 (9–14)
PD ultrafiltration volume (L/24 hours)	1.55±0.58 (0.95–2.6)	1.65±0.76 (1.1–2.55)	1.58±0.32 (1.3–2.1)

8 cases, 12 months

Proactive option, early initiation of PD+HD

Ueda A, 4th ACM-ISPD, Beijing 2009

- Combination initiated at a daily UV more than 700 mL
Five days PD (4 ex, 1.5 L 1.5% G) + 1/wk HD (3 hours) without UF.
- A 57yo DM controlled PD+HD 72 months.
Urinary and PD UF volume were maintained for 72 months, and so UF in the HD session was not necessary, because no weight gain.
- Weekly CCr was not changed at Start and 72 months
 - 62L/wk/1.73m² [23 L (RKF), 29 L (PD), and 10 L (HD)],
 - 71L/wk/1.73m² [33 L (RKF), 28 L (PD), and 10 L (HD)].
- The D/P Cr at the start and end was 0.48 and 0.52 respectively.

Conclusion

- **Advantage of PD means; “Daily dialysis”**
- **Disadvantage of PD**
 - **Low dosage compared to super-high flux HD**
 - **Possibility of peritoneal deterioration on long-term PD**
- **One option for resolve**
 - **Combination therapy PD with HD used biocompatible PD solutions & super-high flux HD membranes**

“High dose daily dialysis”

Question to combination therapy

- ❖ **When should we stop the PD ?**
 - ❖ Combination therapy is able to maintain long-term PD.
 - ❖ The decision of transfer to complete HD is difficult.
- ❖ **We should check the peritoneal deterioration on the combination therapy as well as PD therapy.**
 - ❖ Ie, PET & peritoneal effluent markers, every 6 months.





Thank you for your attention