18th Asian Colloquium in Nephrology

SOTANC

Best Practices in Kidney Care in Asia

19 – 21 July 2019

Incorporating: SOTANC - State-Of-The-Art Nephrology Course (Nursing)
Singapore Society of Nephrology Annual Scientific Meeting
Asia Renal Association - Asian Nephrology Conference

Haemodialysis in the new ESKD patients : Doing Less for More

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Department of Nephrology,

Hospital Kuala Lumpur, MALAYSIA

DEFINITION & HISTORICAL PERSPECTIVES

Incremental Haemodialysis (HD) uses the concept of adjusting dialysis dose according to Residual Kidney Function (RKF) so that the HD dose is individualized.

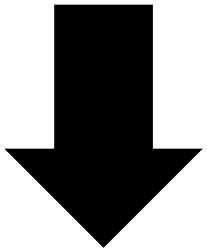
This individualization of HD prescription allows for initial use of

- shorter duration
- less frequent
- less intense dialysis

(e.g. dialyzers with smaller surface areas, and lower blood & dialysate flows)

BASIS for Concept of Incremental HD

Supply sufficient dialysis to remove uremic toxins & control hypervolaemia.



Escalate dose of HD as RRF declines

Historical perspectives

- In the 1960's, hemodialysis treatment was first offered as a life-sustaining treatment in the form of long sessions (≥10 hours) administered every 5 to 7 days.

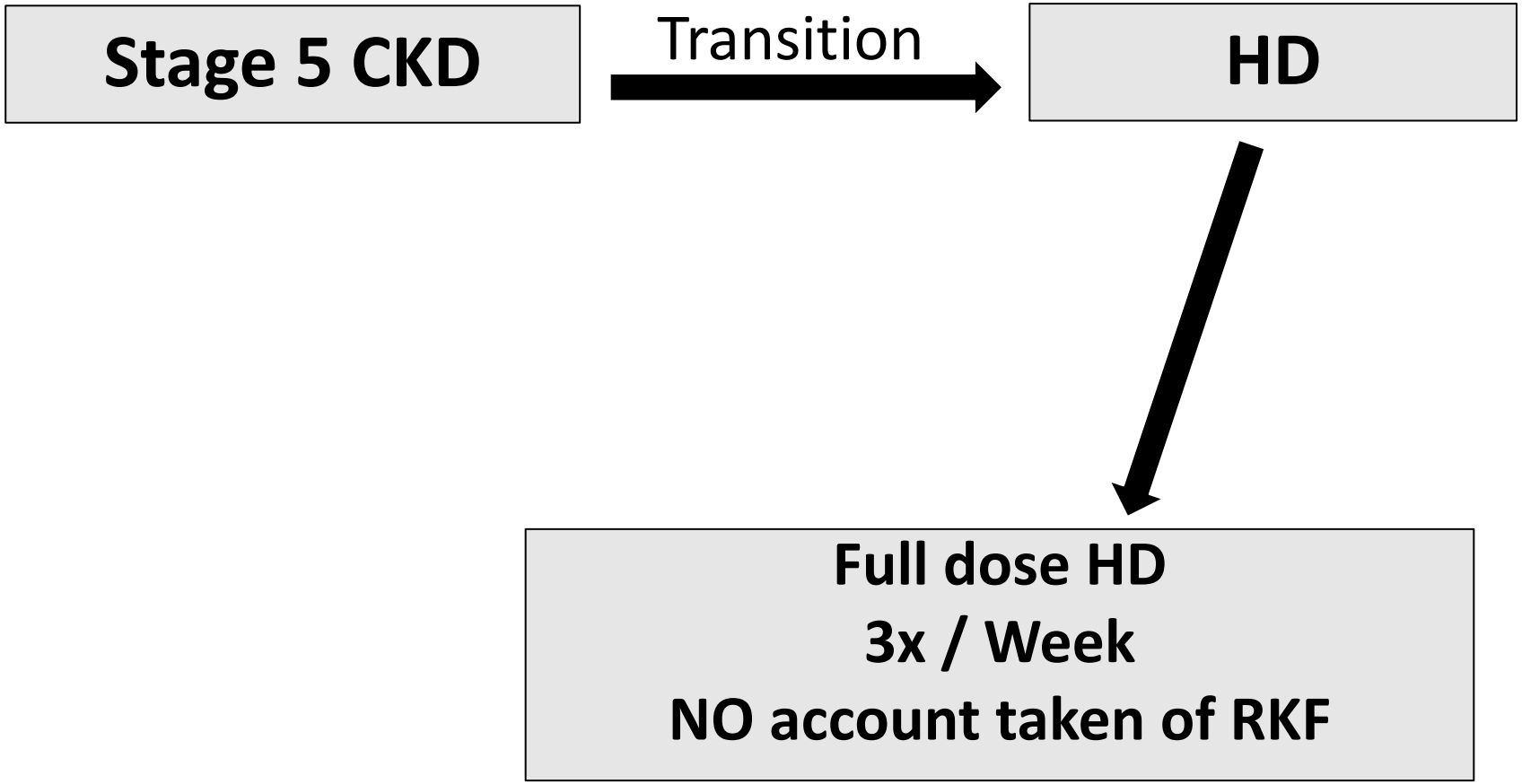
- Subsequently , twice- and then thrice-weekly treatment regimens were developed to prevent uremic symptoms on a long-term basis.

  → Thrice-weekly regimen becoming the ‘standard of care’

  despite a lack of comparative studies

Existing Practice for HD :

Most Clinical Practice Guidelines :



HISTORICAL PRECEDENTS:

Incremental dialysis is well established among PD patients

RKF

- Is routinely measured, has long been utilized in determining the optimal dialysis dose [1]
- has been reported in observational studies as an independent predictor of technique success and survival in PD [2-3]

1. Mehrotra R, Nolph KD, Gotch F.Early initiation of chronic dialysis:role of incremental dialysis. Perit Dial Int. 1997;17:426-430.
2. Bargman JM, Thorpe KE, Churchill DN, Group CPDS. Relative contribution of residual renal function and peritoneal clearance to adequacy of dialysis: a reanalysis of the CANUSA study. J Am Soc Nephrol. 2001;12:2158-2162.
3. . Diaz-Buxo JA, Lowrie EG, Lew NL, Zhang SM, Zhu X, Lazarus JM. Associates of mortality among peritoneal dialysis patients with special eference to peritoneal transport rates and solute clearance. Am J Kidney Dis. 1999;33:523-534.

DICTUMS

I

Thrice weekly HD was established to provide adequate dialysis

>30 yrs ago

" Standard of Care"

II

All landmark trials of HD adequacy * have been anchored to thrice-weekly HD regimes

(albeit in patients with little/no RKF)

III

Recent trials of more frequent HD (FHN trial):

HD 6x a week appeared to confer improved CV & survival benefits

- NCDS – CrCl ≤3 mL/minute
- HEMO - urea clearance ≤1.5 mL/mim/35L BW

KDOQI 2006

- The National Kidney Foundation–Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) 2006 guidelines have suggested a twice-weekly schedule among patients with “substantial residual renal urea clearance (KRU)” (i.e. ≥3.0 mL/min/1.73m^2)

Existing Practice :

Initiation of HD :

USA
>96% on 3x/Weekly

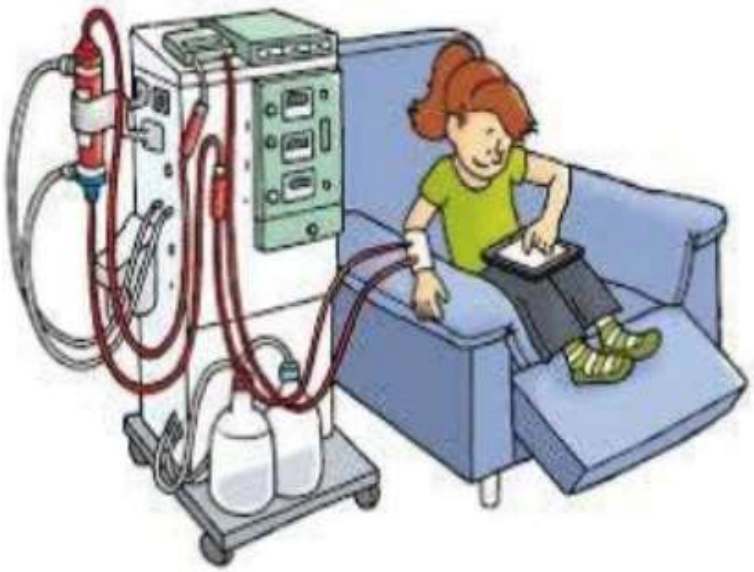
China
26% on 2x/Weekly

Sudan
75% commenced on 2x/Weekly

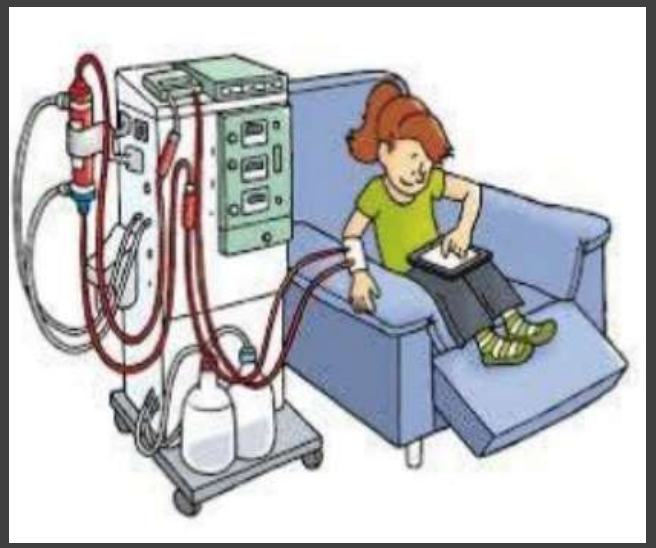
Haemodialysis in the new ESKD patients : Can Less be More ?

NO RCTs comparing twice-weekly with thrice weekly HD

Haemodialysis in the new ESKD patients : Can Less be More ?

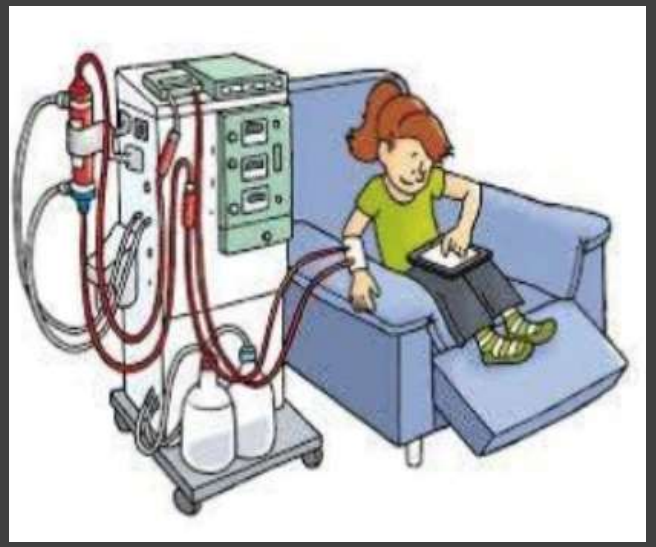


Patient



1. Preservation of residual kidney function (RKF)
2. Longevity of vascular access
3. Better QOL
4. Cost saving

Patient



1. **Preservation of residual kidney function (RKF)**
2. Longevity of vascular access
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4. Cost-saving

DOI: 10.1111/sdi.12701

UNRESOLVED ISSUES IN
THE CARE OF DIALYSIS PATIENTS

Guest Editor: Steven Fishbane

WILEY Seminars in Dialysis 2018

Incremental dialysis for preserving residual kidney function—Does one size fit all when initiating dialysis?

Anna T. Mathew[1] | Yoshitsugu Obi[2] | Connie M. Rhee[2] | Jason A. Chou[2] | Kamyar Kalantar-Zadeh[2,3,4]

Narrative review of 12 *observational cohort* studies of twice-weekly compared to thrice-weekly HD.

TABLE 1 Summary of comparative studies evaluating patient outcomes in with twice- vs thrice-weekly hemodialysis

RRF

Author	Year	Study design	Study duration (y)	Twice-weekly N	Thrice-weekly N	RKF Metric	Results		
							RKF	Mortality	Other
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Elamin[82]	2012	Prospective cohort	2	Total cohort N = 1011 74.8% 2x week		-	-	Similar one year mortality in twice-weekly group (85% vs 89%, *P* = .06)	-
Fernandez-Lucas[57]	2012	Prospective cohort	5	41	54	Loss of UOP/ 24 hours	Loss of UOP/24 hours was greater in thrice-weekly group compared to twice-weekly group (206 mL/ month vs 91 mL/month	Survival greater in twice-weekly group (log-rank 3.96; *P* = .04)	-
Zhang[55]	2014	Prospective cohort	1	30	55	RKF loss, defined as < 200 mL/d of urine output	RKF loss reported in 60% (n = 18) in twice-weekly vs 82% (n = 45) in thrice-weekly group	-	-

RRF

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Lin[54]	2009	Prospective Cohort	8	23	51	UOP and residual GFR[b]	Twice-weekly group had higher mean urine output than thrice-weekly group (1.7 L vs 0.61 L; P = .001) and residual GFR (1.9 mL/min vs 0.71 mL/min; P = .001)	–	Less frequent hospitalization in twice-weekly group (63% vs 33%; P = .012 No difference in nutrition or inflammation indices between groups
Stankuviene[80]	2010	Retrospective cohort	8	Total cohort N = 2428 58.5% 3x week 36.2% 2x week 5.3% 1x week		–	–	Higher mortality in twice-weekly group (RR 1.98 (95% CI 1.64, 2.40; P < .001)	–

RRF

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Obi[28]	2016	Retrospective cohort	4	351	8068	UOP and KRU +	Slower RKF decline over time in twice vs thrice-weekly group (UOP to ≤600 mL/d RR 1.15 (95% CI, 1.02-1.30, P < .001)	Similar overall survival between groups (HR 1.11; 95% CI, 0.89-1.38; P = .3).	-
Hwang[83]	2016	Prospective cohort	3	113	572	KRU corrected for 1.73 m^2 body surface area +	RKF at 36 months 2.9 mL/min in twice-weekly vs 1.0 mL/min in thrice-weekly; P < .001)	Higher mortality in twice-weekly group compared to thrice-weekly group (HR 4.2; 95% CI 1.02-17.32; P = .04)	-
Mathew[58]	2016	Retrospective cohort	5	434	50162	-	-	Similar survival between groups (HR 0.88, 95% CI 0.72, 1.08), after adjustment for RKF	-

RKF, residual kidney function; eGFR, estimated glomerular filtration rate; UOP, urine output; KRU, residual urea clearance; GFR, glomerular filtration rate; RR, relative risk; CI, confidence interval.

[a]Includes once-weekly and twice-weekly HD patients, 5.3% and 36.2% of total cohort, respectively.

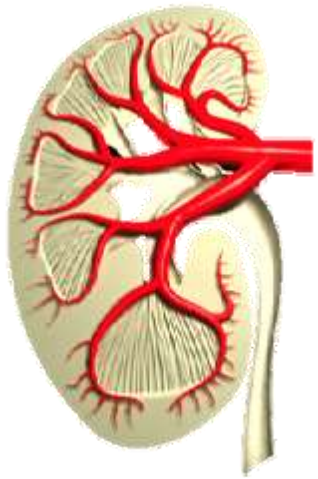
[b]Calculated as arithmetic mean of residual urea and creatinine clearances.

Benefits of RKF:

1. Better clearance of larger middle molecules
   eg β2 microglobulin

2. Better clearance of cytokines (TNF α , IL-1)

3. Regulates fluid & electrolyte balance → more liberal dietary intakes



4. Better nutritional status

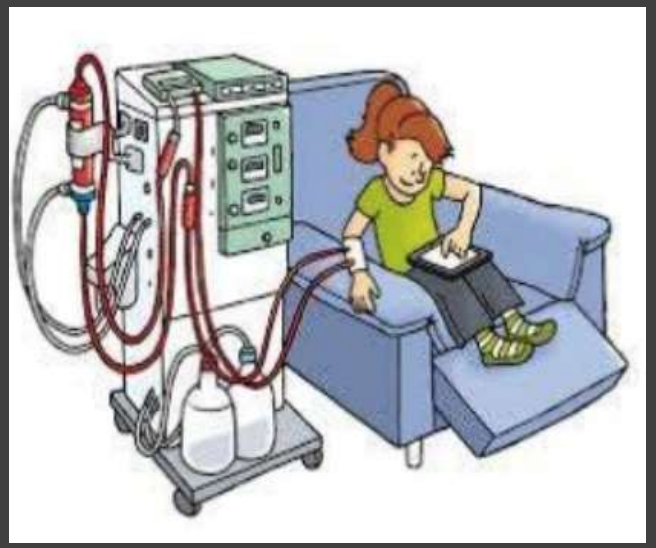
Benefits of RKF:

5. Improved anaemia control.

6. Improved bone mineral metabolism

7. Reduced LVH & mortality

Patient



1. Preservation of residual kidney function (RKF)
2. **Longevity of vascular access**
3. Better QOL
4. Cost saving

Preservation of vascular access

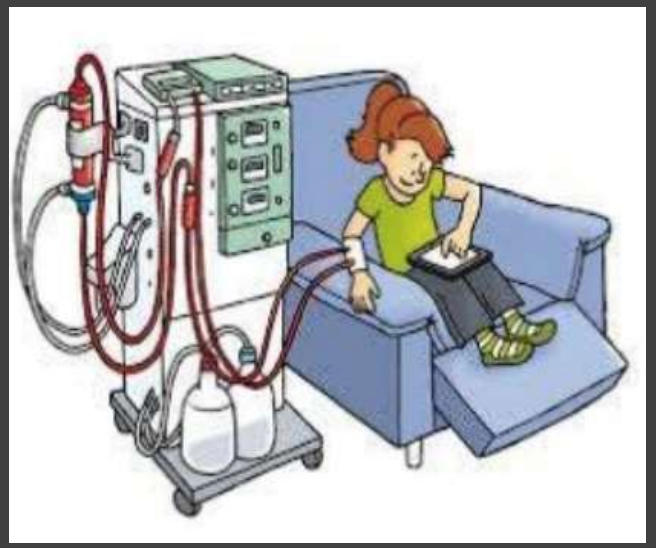
- Less frequent arteriovenous fistula or graft cannulations may increase longevity of vascular access .

- In an analysis from the FHN study, more frequent HD was associated with higher risk of vascular complications including repair, loss, or vascular access related hospitalization

- In new ESKD patients, incremental HD could be viewed as a form of “breaking-in” the access, in particular those with fragile or otherwise tenuous dialysis vascular accesses

Kalantar-Zadeh et al AJKD 2014

Patient



1. Preservation of residual kidney function (RKF)
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3. **Better QOL**
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QOL …. Robust prospective studies are lacking

Nephrol Dial Transplant (2014) 29: 1770–1777
doi: 10.1093/ndt/gft472
Advance Access publication 8 December 2013

ndt
Nephrology Dialysis Transplantation

Original Article

Two-times weekly hemodialysis in China: frequency, associated patient and treatment characteristics and Quality of Life in the China Dialysis Outcomes and Practice Patterns study

Brian Bieber[1*], Jiaqi Qian[2,*], Shuchi Anand[3], Yucheng Yan[2], Nan Chen[4], Mia Wang[1], Mei Wang[5], Li Zuo[6,7], Fan Fan Hou[8], Ronald L. Pisoni[1], Bruce M. Robinson[1] and Sylvia P.B. Ramirez[1]

In 304 patients on a twice-weekly HD regimen and 982 patients on a thrice-weekly regimen, there was NO significant difference in HRQOL, measured using the KDQOL SF 12

Less HD = **More** cost savings for patients

In many countries in less economically privileged areas

- co-payments for HD therapy are required
- need to consider indirect costs e.g. for travel
  (unlike developed countries which provide ambulance services etc to transport patients to HD units)
- preserved RKF→ ↓ requirement for medications to treat anaemia and CKD-MBD

Health care Providers

1. Easier to persuade patients to initiate dialysis

2. Helps build doctor-patient relationship because you are listening to their preferences, personalising their Rx

I don't care what day it is.
Four hours is four hours.

Healthcare Systems

1. LESS HD = MORE MONEY

- **↓ dialysis procedures/ transportation costs**
- **? ↓ no. of dialysis stations**
- **↓ dialysis access costs through preservation of vascular access (next leading expense after dialysis costs & hospitalization)**

2. SHARE LIMITED RESOURCES BETWEEN MORE PATIENTS

- IN PRACTICE , helps to ration out the limited buffer HD slots for unplanned HD starters while looking for permanent HD slots/ waiting to start PD

POTENTIAL RISKS

1. Underdialysis due to unrecognized loss of kidney function.
2. Reluctance to increase to thrice-weekly HD when needed.
3. Possible increased risk of Heart failure
4. Decline in nutritional status
5. Increased risk of HTN, HyperPO_4, Hyperkalemia & Mortality.

ORIGINAL ARTICLE FREE PREVIEW

Long Interdialytic Interval and Mortality among Patients Receiving Hemodialysis

Robert N. Foley, M.B., David T. Gilbertson, Ph.D., Thomas Murray, M.S., and Allan J. Collins, M.D.

September 22, 2011
N Engl J Med 2011; 365:1099-1107
DOI: 10.1056/NEJMoa1103313

Abstract

BACKGROUND Patients with end-stage renal disease requiring dialysis have limited tolerance of metabolic and volume-related deviations from normal ranges; in addition, the prevalence of cardiovascular disease is high among such patients. Given these problems, we hypothesized that a long interdialytic interval is associated with adverse events in patients receiving hemodialysis.

- All-cause mortality was significantly higher on the day after the long, 2-day interdialytic interval compared to other days (22.1 vs 18.0 deaths per 100 person years, P < .001).

Am J Kidney Dis. 2017 Jul;70(1):21-29. doi: 10.1053/j.ajkd.2016.10.024. Epub 2017 Jan 19.

Serum Potassium and Short-term Clinical Outcomes Among Hemodialysis Patients: Impact of the Long Interdialytic Interval.

Brunelli SM[1], Du Mond C[2], Oestreicher N[3], Rakov V[4], Spiegel DM[2].

Author information

Abstract

BACKGROUND: Hyperkalemia is common among hemodialysis patients and is associated with morbidity and mortality. The long interdialytic interval is likewise associated with adverse outcomes. However, the interplay among serum potassium, dialysis cycle phase, and clinical outcomes has not been examined.

STUDY DESIGN: Retrospective observational study.

SETTING & PARTICIPANTS: 52,734 patients receiving in-center hemodialysis at a large dialysis organization during 2010 and 2011 contributed 533,889 potassium measurements (230,634 on Monday; 285,522 on Wednesday; 17,733 on Friday).

PREDICTOR: Serum potassium concentration, day of the week of potassium measurement.

OUTCOMES: Death, hospitalization, emergency department (ED) visit.

CONCLUSIONS: Higher serum potassium is associated with increased short-term risk of hospitalization, ED visit, and death. The association between serum potassium and hospitalization risk is modified by day of the week, consistent with a contribution of accumulated potassium to adverse outcomes following the long interdialytic interval. Further work is needed to determine whether directed interventions ameliorate this risk.

- The cohort in both studies was prevalent HD patients, who likely had minimal /nonexistent RKF

- Incident HD patient would usually still have substantial RKF which may mitigate the rapid UF and electrolyte shifts after a long interdialytic interval

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- **Variable effect of incremental HD on mortality may be related to**

? a beneficial modifying effect of RKF, which is not accounted for in all studies.

? confounding by indication b/c healthier patients are put on less frequent HD

- **Note : these are only associations from observational studies.**

Hospitalisation

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ea clearance; GFR, glomerular filtration rate; RR, relative risk; CI, confidence interval.

NUTRITION

omes in with twice- vs thrice-weekly hemodialysis

					Thrice-weekly N	RKF Metric	Results: RKF	Results: Mortality	Results: Other
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Incremental HD – pros and cons

Benefits :

- Preservation of RKF
- Extending the event-free life of arteriovenous fistulas and grafts
- ± Patient survival and Quality of Life - variable associations
- Reduction in costs

Potential Risks

- Increased hospitalization and mortality, perhaps related to fluid and electrolyte shifts after a long interdialytic interval

Candidates for Incremental HD

Treatment Criteria for 2x/wk HD

1	Good RKF with a urine output >0.5 L/day
2	Limited fluid retention between 2 consecutive HD treatments with a fluid gain <2.5 kg (or less than 5% of the ideal dry weight) without HD for 3 to 4 days
3	Limited or readily manageable cardiovascular or pulmonary symptoms without clinically significant fluid overload**
4	Suitable body size relative to RKF; patients with larger body size may be suitable for 2x/wk HD if not hypercatabolic
5	Hyperkalemia (K, >5.5 mEq/L) is infrequent or readily manageable
6	Hyperphosphatemia (P, >5.5 mg/dL) is infrequent or readily manageable
7	Good nutritional status without florid hypercatabolic state
8	Lack of profound anemia (Hb >8 g/dL) and appropriate responsiveness to anemia therapy
9	Infrequent hospitalization and easily manageable comorbid conditions
10	Satisfactory health-related quality of life

Kalantar-Zadeh et al, AJKD 2014

IN ADDITION …..

- RKF, patient symptoms and interdialytic weight gains, must be regularly monitored

- Monthly timed urine collections for residual creatinine and urea clearance are advised

  Alternative : urine volume as a surrogate measure

(Kalantar-Zadeh et al. AJKD 2014;64:181-186)

AND .....

- Adjustment to the HD prescription should be made

- as RKF declines

- and/or with a change in patient factors.

Incremental HD

Benefits :

- preservation of RKF
- Extending the event-free life of arteriovenous fistulas and grafts

- Patient survival and quality of

life, however, has been variably associated with incremental HD.

Potential Risks

- increased hospitalization and mortality, perhaps related to fluid and electrolyte shifts after a long interdialytic interval

Barriers

- Logistics of arranging shifts to maximise HD machine use /loss of income (private sector)
- Adminstrative complexity of billing

Solution : attention to scheduling eg Mon-Thurs, Tues-Fri, Wed-Sat.
= 3 pts x HD 2x/wk = 2 pts x HD 3x/wk

Risk that patients may refuse to increase HD prescriptions

- Clinicians must set out clear expectations prior to incremental HD initiation to ensure a smooth patient transition from twice to thrice-weekly HD when this becomes necessary

  ? Patient contract

Conclusion (1)

- Incremental individualized HD therapy may prove to be the most appropriate approach for new ESKD patients starting their dialysis journey

- Doing “less” may be “more” for carefully selected (and monitored) new ESKD patients

Conclusion (2)

- Evidence so far is limited to large observational studies in select populations

- Well-designed clinical trials are still needed to determine the safety, efficacy, and optimal patient characteristics to optimize outcomes with an incremental HD approach

Conclusion (3)

- “PD first” should be the preferred mode of dialysis for most new ESKD patient, given consistent data demonstrating an association between PD, preservation of RKF & survival

- For new ESKD patients with terminal conditions, may need to consider more conservative and palliative options rather than incremental dialysis

Thank YOU


SAVE THE DATE
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AKI
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26 JULY 2019
Abstract Submission Deadline
26 AUGUST 2019
Early Bird Registration Deadline
26 SEPTEMBER 2019
Online Registration Closing Date
www.apcrrt.com
apcrrt2019@crestevendz.com.my

Adequacy Targets :

GUIDELINE 4. MINIMALLY ADEQUATE HEMODIALYSIS

4.1 Minimally adequate dose:
The minimally adequate dose of HD given 3 times per week to patients with K_r less than 2 mL/min/1.73 m^2 should be an spKt/V (excluding RKF) of 1.2 per dialysis. For treatment times less than 5 hours, an alternative minimum dose is a URR of 65%. (A)

4.2 Target dose:
The target dose for HD given 3 times per week with K_r less than 2 mL/min/1.73 m^2 should be an spKt/V of 1.4 per dialysis not including RKF, or URR of 70%. (A)

4.3 In patients with residual urea clearance (K_r) greater than or equal to 2 mL/min/1.73 m^2, the minimum session spKt/V can be reduced. One method of minimum dose reduction is described in CPR 4.4. In such patients, the target spKt/V should be at least 15% greater than the minimum dose. (B)

4.4 Missed and shortened treatments:
Efforts should be made to monitor and minimize the occurrence of missed or shortened treatments. (B)

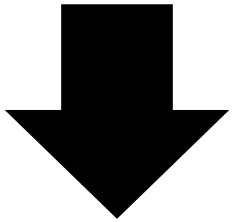
versus mortality based on either the USRDS-Medicare data set or the Fresenius Medical Care subset of these data.[102-104]

HEMO Clinical Study: Primary (Randomized) Results

Primary results of the HEMO Study, which randomized patients to a delivered eKt/V of 1.16 versus 1.53, equivalent to URR values of about 63% versus 75% or spKt/V values of about 1.3 versus 1.7, revealed little evidence to support increasing the dose of dialysis beyond the current (2000) KDOQI recommendations, respectively.[6] The lack of benefit, without even a trend that was close to statistical significance, appeared not only in the primary outcome of mortality, but also in a variety of main secondary composite outcomes relating to various causes of hospitalization combined with mortality. Furthermore, analysis of minor secondary composite outcomes dealing with nutritional measures—including changes in weight and serum albumin levels,[105] as well as QOL measures[106]—also failed to support a beneficial effect of increasing

KDOQI Guidelines (1997)

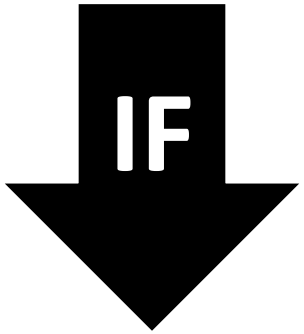
GFR reaches 10ml/min/1.73m^2



Start Dialysis

Revised KDOQI Guidelines (2006)

Dialysis initiation warranted if
GFR < 15ml/min/1.73m^2



Uremic symptoms or Declining health

- In the Frequent Hemodialysis Network (FHN) Daily Trial, which showed reduced left ventricular hypertrophy and better survival in patients with frequent in-center hemodialysis, most patients had dialysis vintages ≥2 years and two-thirds of patients were anuric.11,12
- In contrast, in the FHN Nocturnal Trial, where higher mortality was observed in the frequent nocturnal hemodialysis group, patients had comparatively shorter dialysis vintages (approximately 1 year in median), and about half of patients had urine volume >500 mL/day.13-15

Incremental dialysis: review of recent literature

Thomas A. Golper

Curr Opin Nephrol Hypertens 2017, 26:000–000

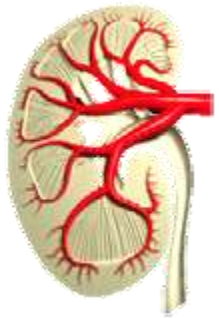
" A weekly standardized Kt/V perhaps of 1.8– 2.0 seems reasonable in some selected patients and there are no clear data to declare a minimum of 2.1 as the 2015 KDOQI Guidelines have suggested "

" KDOQI Guidelines are for clinicians…..The 2015 document states that they are neither intended as a standard of care nor should they be construed as one."

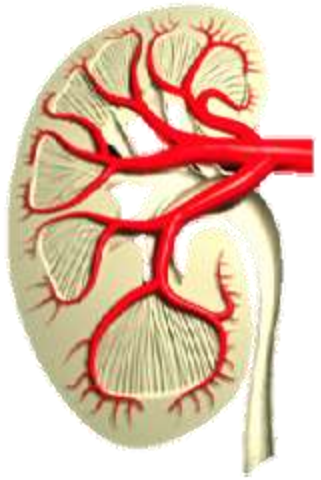
DEFINITION & HISTORICAL PERSPECTIVES

1. Residual Renal Function (RRF)
   = the residual GFR in patients with ESRD,
   in particular those receiving RRT.

2. Decline in RRF is noted in patients on dialysis
   as renal parenchyma is lost with time.



IMPLEMENTATION OF INCREMENTAL HD



1
Measure and Monitor RKF

- Measure KRU and/or inter-dialytic UV in all patients initiating hemodialysis
- Target KRU > 3mL/min/1.73m^2 and UV> 0.6L/day
- Monitor KRU and/or UV every month to every quarter in year 1, then every quarter to every 6 months, until UV <100 mL/day or KRU < 2mL/min/1.73m^2
- Measure and monitor other parameters of adequacy (anemia, fluid gains, phosphate/potassium control, nutritional status and health-related quality of life)

2

Avoid or minimize nephrotoxic events

- Radiocontrast dye
- Aminoglycosides
- NSAIDS & COX-2 inhibitors
- Withdrawal of transplant immunosuppression

3

Control Blood Pressure and Avoid Intradialytic Hypotension

- Control Hypertension
- Utilize RAAS blockade and loop diuretics

4
Adjust Hemodialysis Prescription

- Initial dialysis modality (2x weekly HD or PD first approach)
- Re-evaluate dialysis dose if RKF or adequacy changes
- High-flux, biocompatible dialyzer membranes
- Ultrapure water for dialysate
- Avoid intra-dialytic hypotension

5
Consider Low Protein Diet

- Low protein diet (0.6 to 0.7 g/kg/day) on non-dialysis and regular to high protein diet (1.2 g/kg/day) on hemodialysis days

Residual Renal Function

2 essential components of RRF

I	II
Renal clearance of uremic toxins	Urinary Volume (seen as increasingly important)

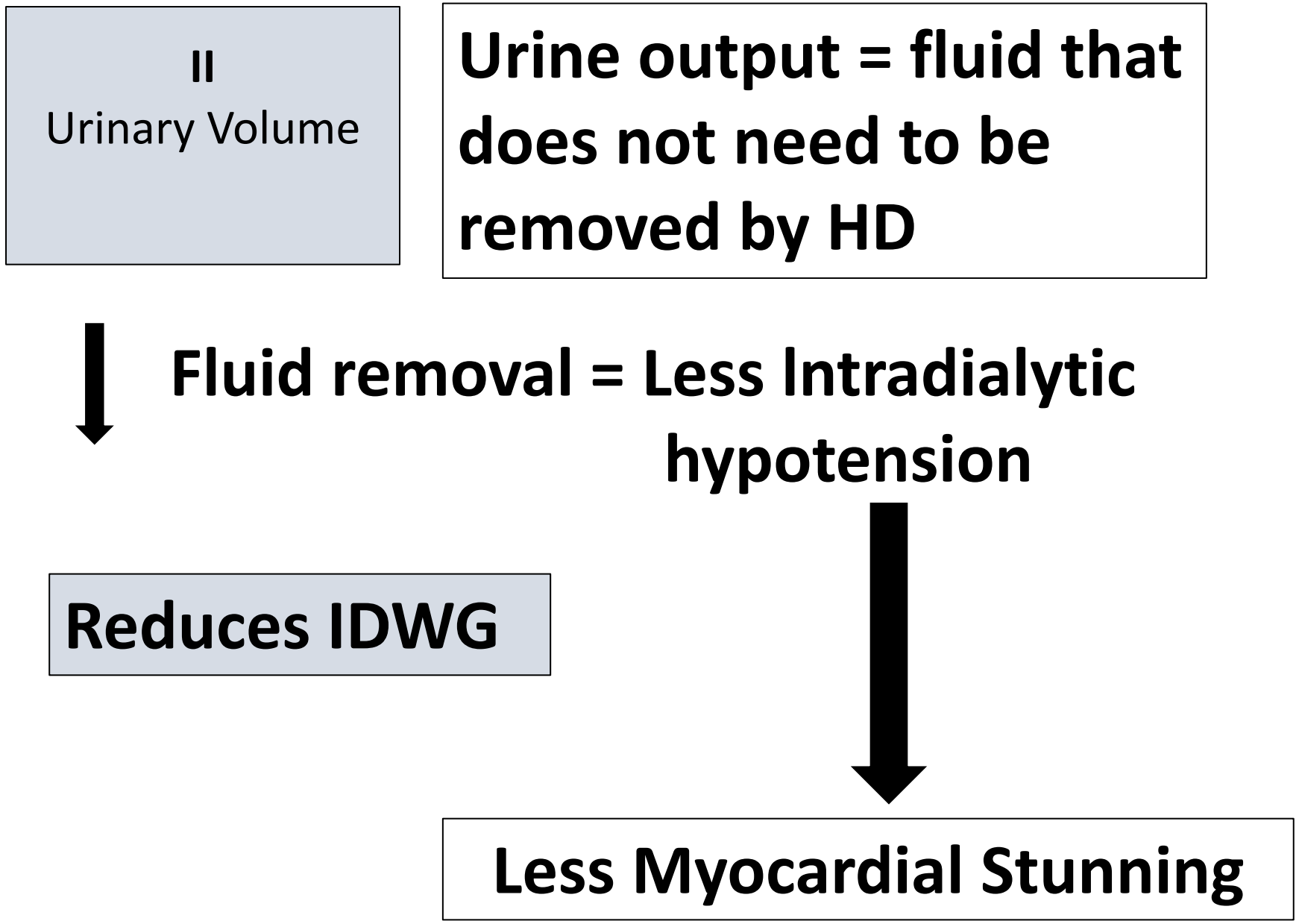
I

Renal clearance of uremic toxins

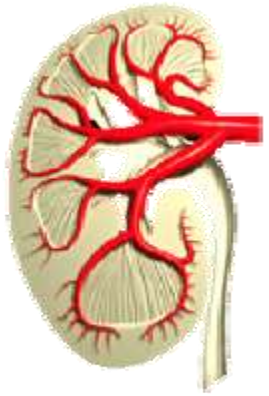
HD = 12 Hours / Week

Native Kidneys GFR is 5ml/min

Significant contribution to removal of toxins as filtration is continous


II
Urinary Volume
Urine output = fluid that does not need to be removed by HD
Fluid removal = Less Intradialytic hypotension
Reduces IDWG
Less Myocardial Stunning

Factors affecting RRF



Factors affecting RRF:

1. Intradialytic Hypotension & Post Dialysis hypovolemia.

Myocardial, mesenteric and cerebrovascular ischemia

Decreased renal perfusion & loss of RRF

Factors affecting RRF:

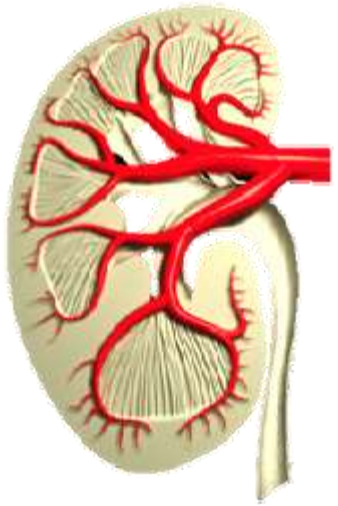
2. Release of nephrotoxic mediators during HD procedure.

3. Reduction in UREA = Reduction in osmotic diuresis

4. Deactivation of remaining nephrons.

5. Nephrotoxic drugs.

Measurement of RRF



Measurement of RRF

1. Gold Standard = Inulin clearance

2. KRU (Residual Renal UREA clearance)

$$KRU = \frac{\text{Urinary Urea (mg/dl) x U vol (mls)}}{\text{Collected time(mins) x [0.9x BU mg/dL]}}$$

Measurement of RRF

3. eGFR (EBPG)

Average of urea + Creatinine Clearance

GFR = $\mathbf{C}_{urea} + \mathbf{C}_{creat} / \mathbf{2}$

4. Urine Volume

- Used in Observational studies
- Does correlate with patient outcomes.

Patient characteristics which may predict favorable outcomes with an incremental approach to HD :

- substantial RKF
- adequate volume control
- lack of significant anemia/electrolyte imbalance
- satisfactory health-related quality of life
- low comorbid disease burden
- good nutritional status without evidence of hypercatabolism.

Mathew et al, Seminars in Dialysis 2018

POTENTIAL BENEFITS

1. Decreased frequency of HD sessions
2. Shorter HD sessions (Frequency & length of HD are frequent patients complaints)
3. Fewer HD access complications
4. Better preservation of RRF
5. Better QoL
6. Decreased Mortality

Nephrol Dial Transplant (2011) 26: 2978–2983
doi: 10.1093/ndt/gfq856
Advance Access publication 11 February 2011

Full loss of residual renal function causes higher mortality in dialysis patients; findings from a marginal structural model

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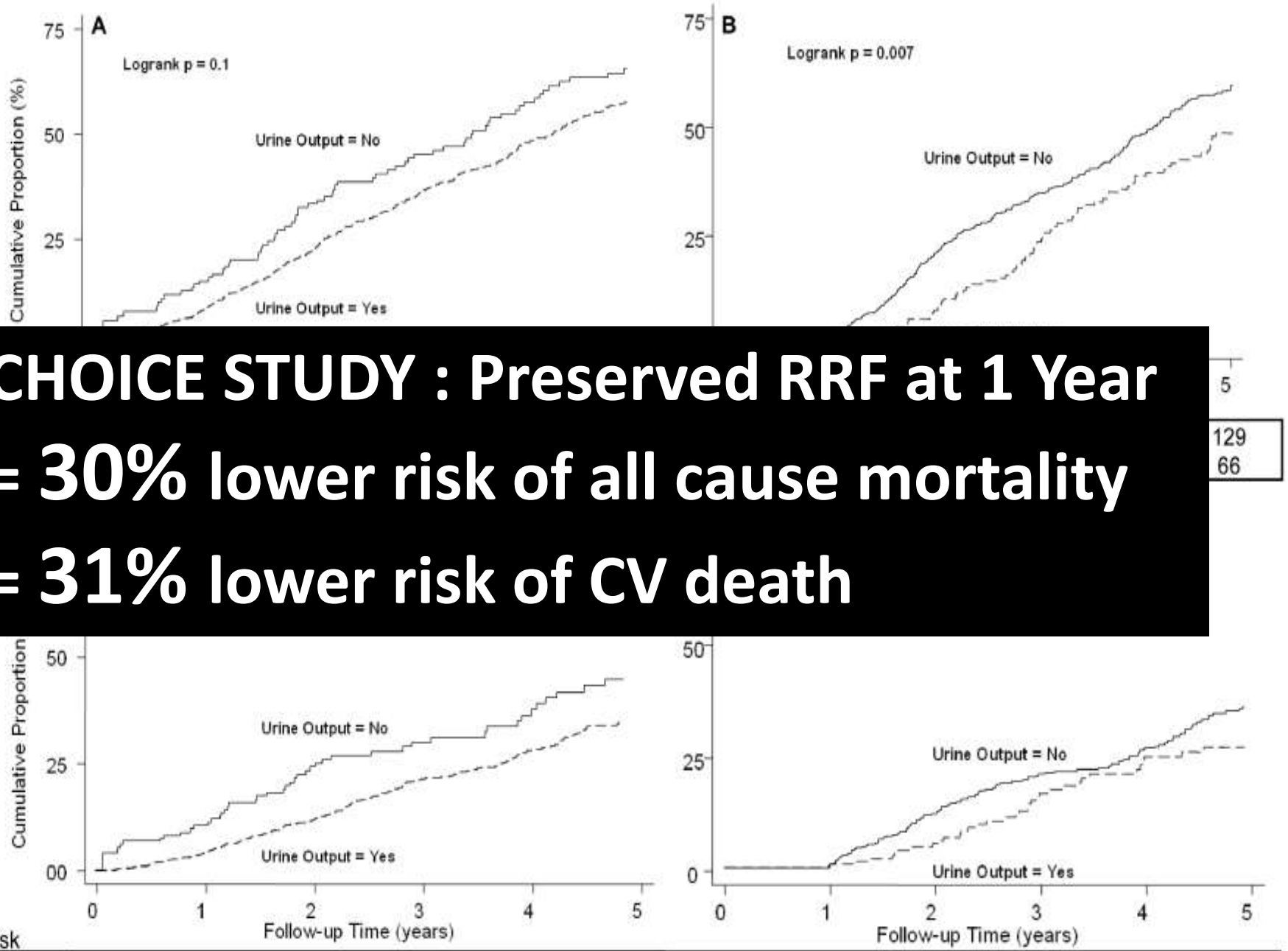
Association of Residual Urine Output With Mortality, Quality of Life, and Inflammation in Incident Hemodialysis Patients: The Choices for Healthy Outcomes in Caring for End-Stage Renal Disease (CHOICE) Study

Tariq Shafi, MBBS, MHS,[1,2] Bernard G. Jaar, MD, MPH,[1,2,3,4] Laura C. Plantinga, ScM,[5] Nancy E. Fink, MPH,[1,3] John H. Sadler, MD,[6] Rulan S. Parekh, MD, MS,[1,3,7] Neil R. Powe, MD, MPH, MBA,[1,3,5] and Josef Coresh, MD, MHS, PhD[1,2,3,8]



No. at risk

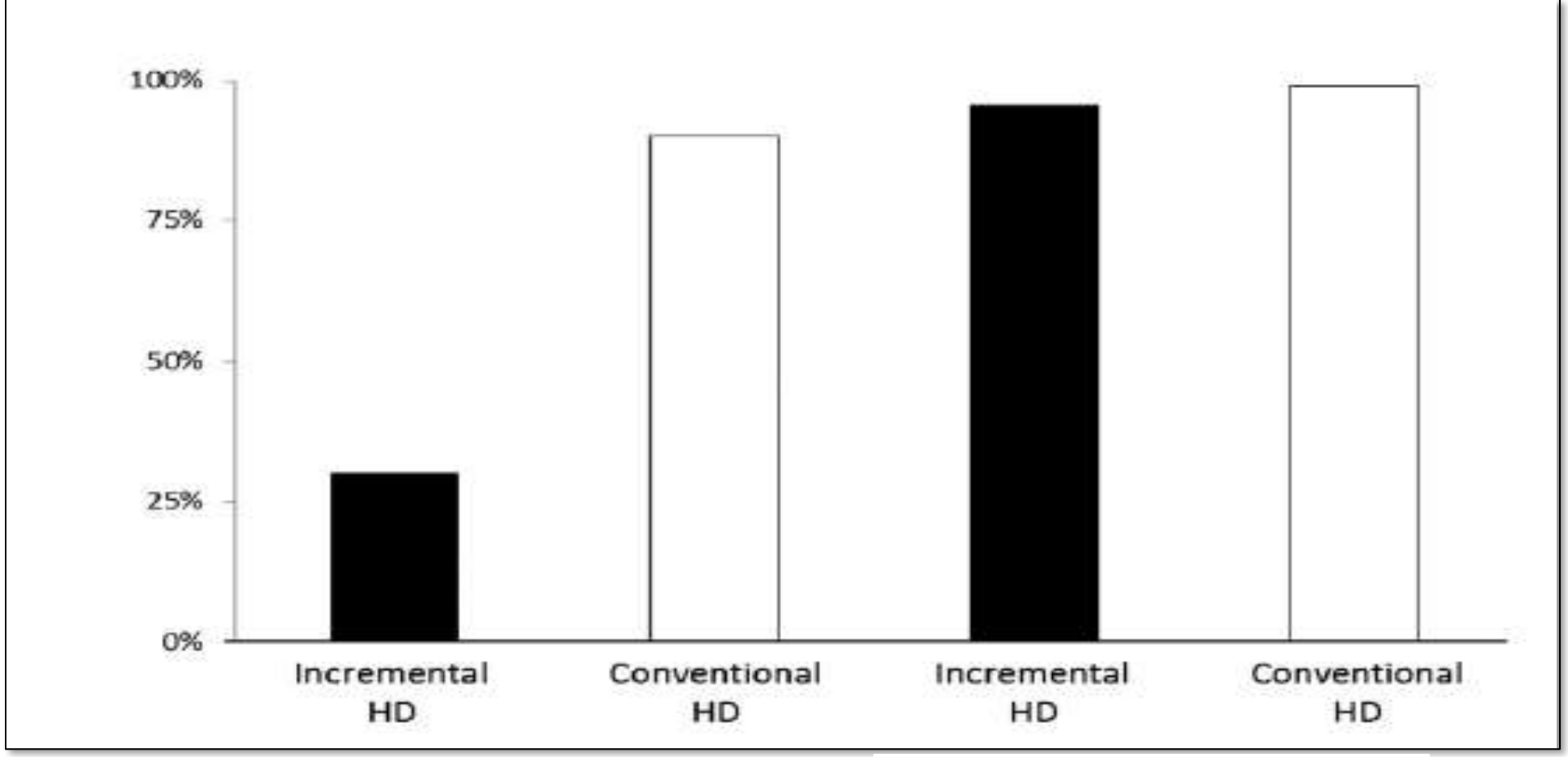
Urine ouput = No	117	97	73	57	43	32		416	311	244	180	129
Urine ouput = Yes	617	541	428	334	248	185		163	142	113	84	66

AJKD

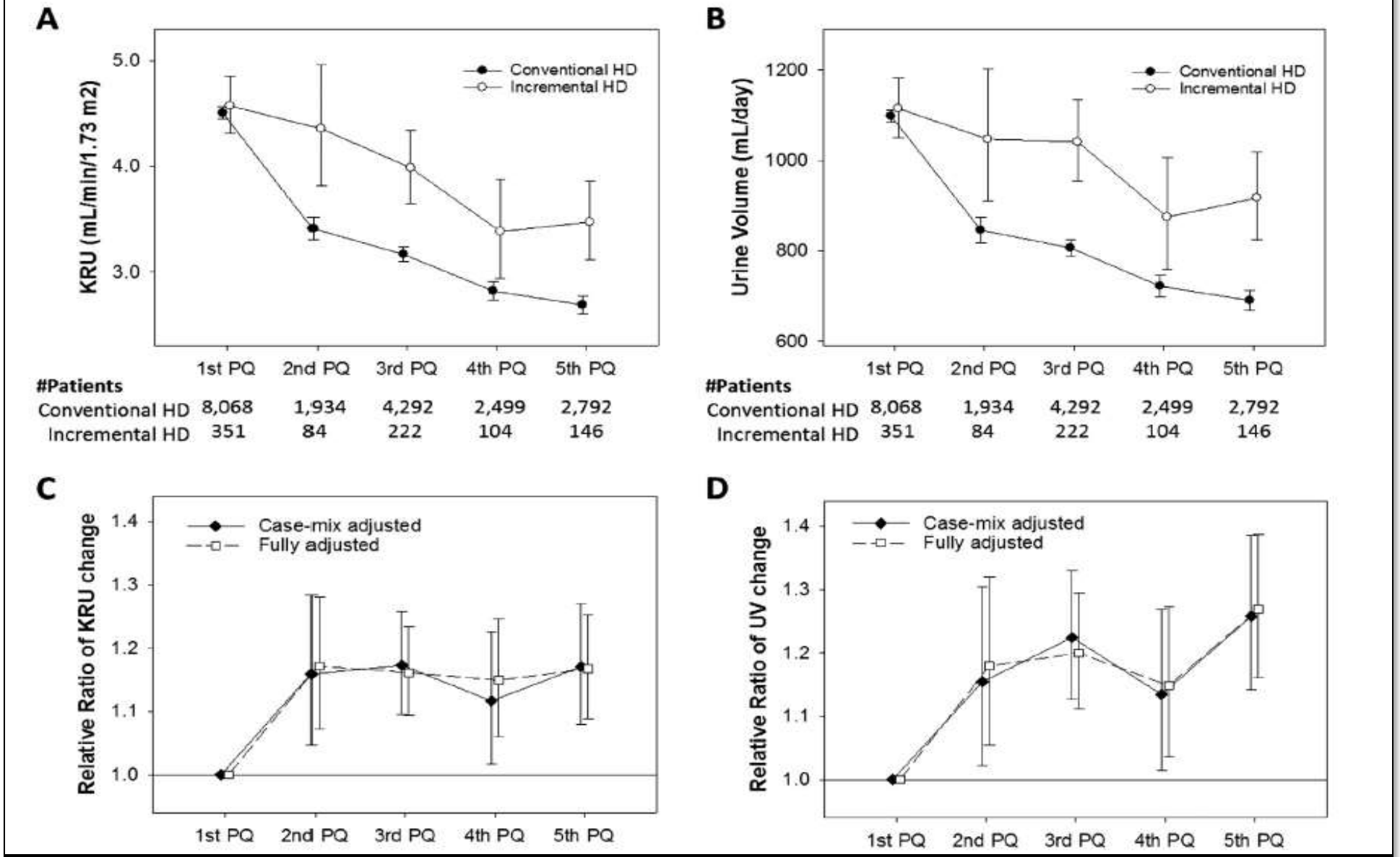
Original Investigation

Incremental Hemodialysis, Residual Kidney Function, and Mortality Risk in Incident Dialysis Patients: A Cohort Study

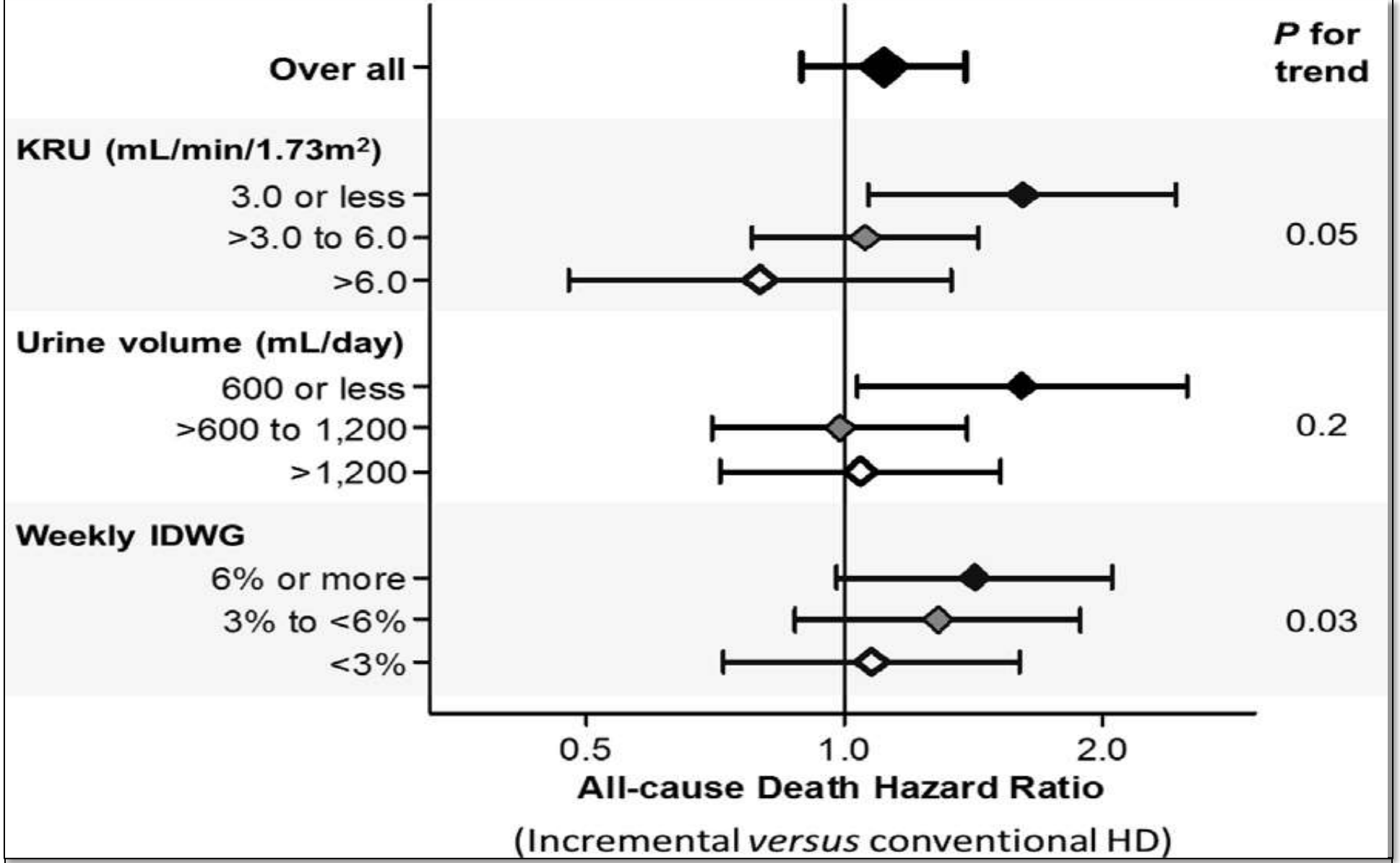
Yoshitsugu Obi, MD, PhD,[1] Elani Streja, MPH, PhD,[1] Connie M. Rhee, MD, MSc,[1] Vanessa Ravel, MPH,[1] Alpesh N. Amin, MD, MBA,[2] Adamasco Cupisti, MD,[3] Jing Chen, MD, PhD,[4] Anna T. Mathew, MD, MPH,[5] Csaba P. Kovesdy, MD,[6,7] Rajnish Mehrotra, MD,[8] and Kamyar Kalantar-Zadeh, MD, MPH, PhD[1,9,10]



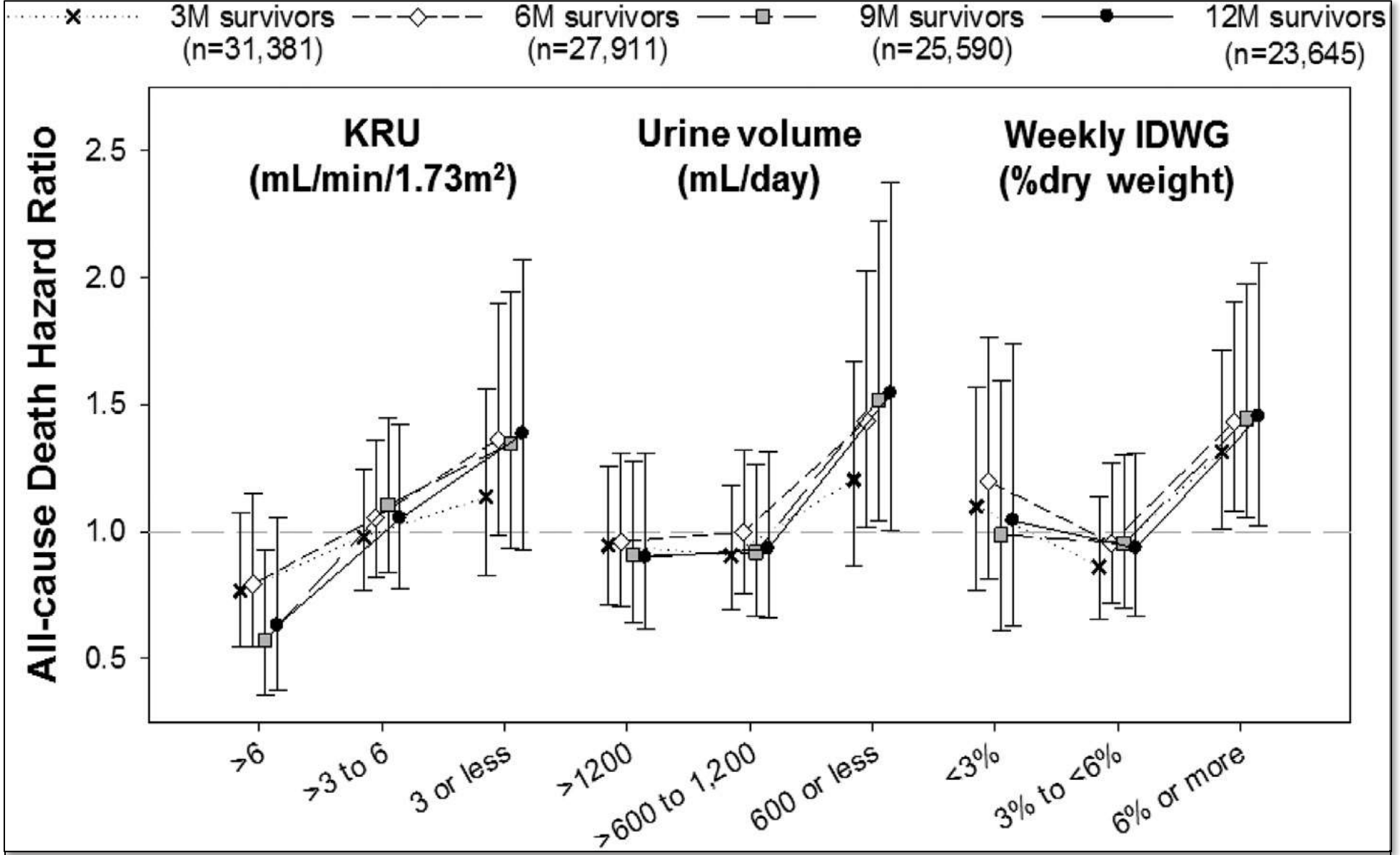
Achievement rate of the minimum total standard Kt/V>2.1 among patients with the incremental and conventional hemodialysis (HD), stratified by renal urea clearance (KRU).



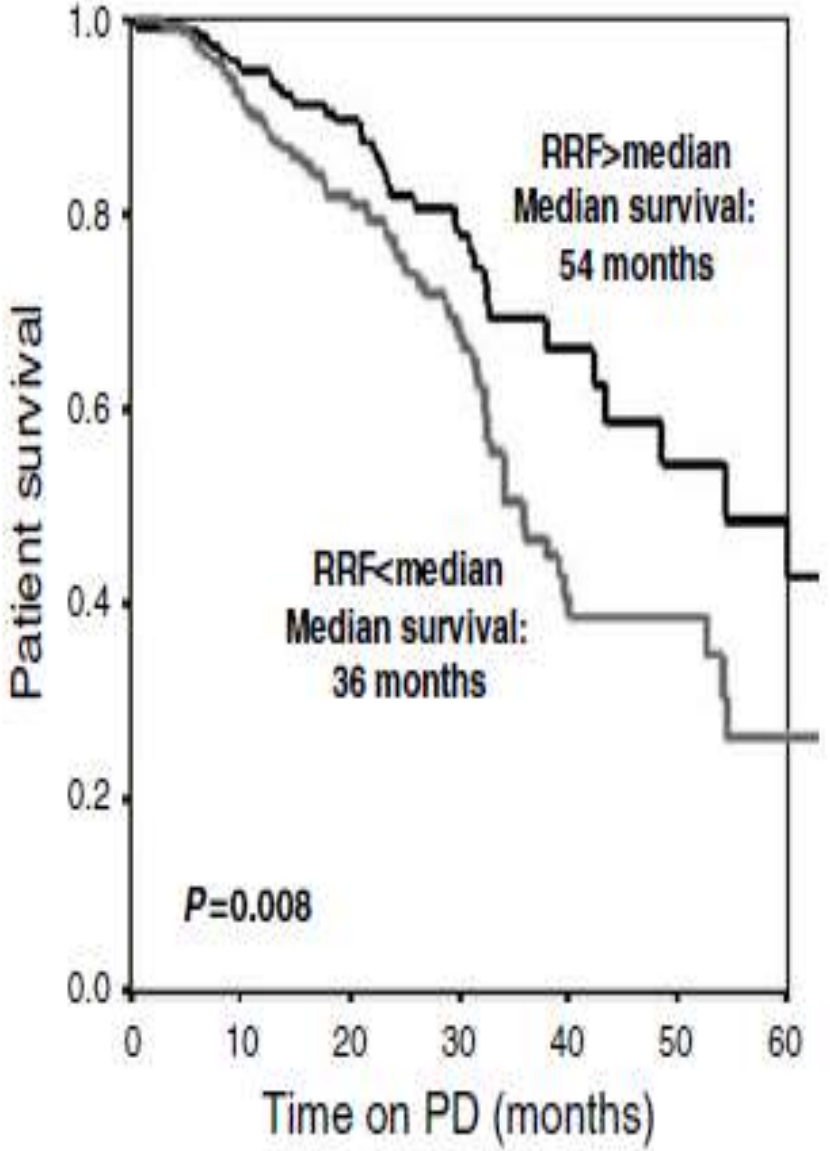
Trends over time of the mean and relative ratio of residual kidney function in the matched cohort of 8,419 patients across 5 patient-quarters (PQs; the conventional vs incremental hemodialysis [HD] regimen). Analyses of (A, C) renal urea clearance (KRU) and (B, D) urine volume (UV). Data are based on weighted match according to baseline KRU and UV, as well as age, sex, race, central venous catheter as vascular access, and history of diabetes. Points and error bars represent point estimates and 95% confidence intervals, respectively.

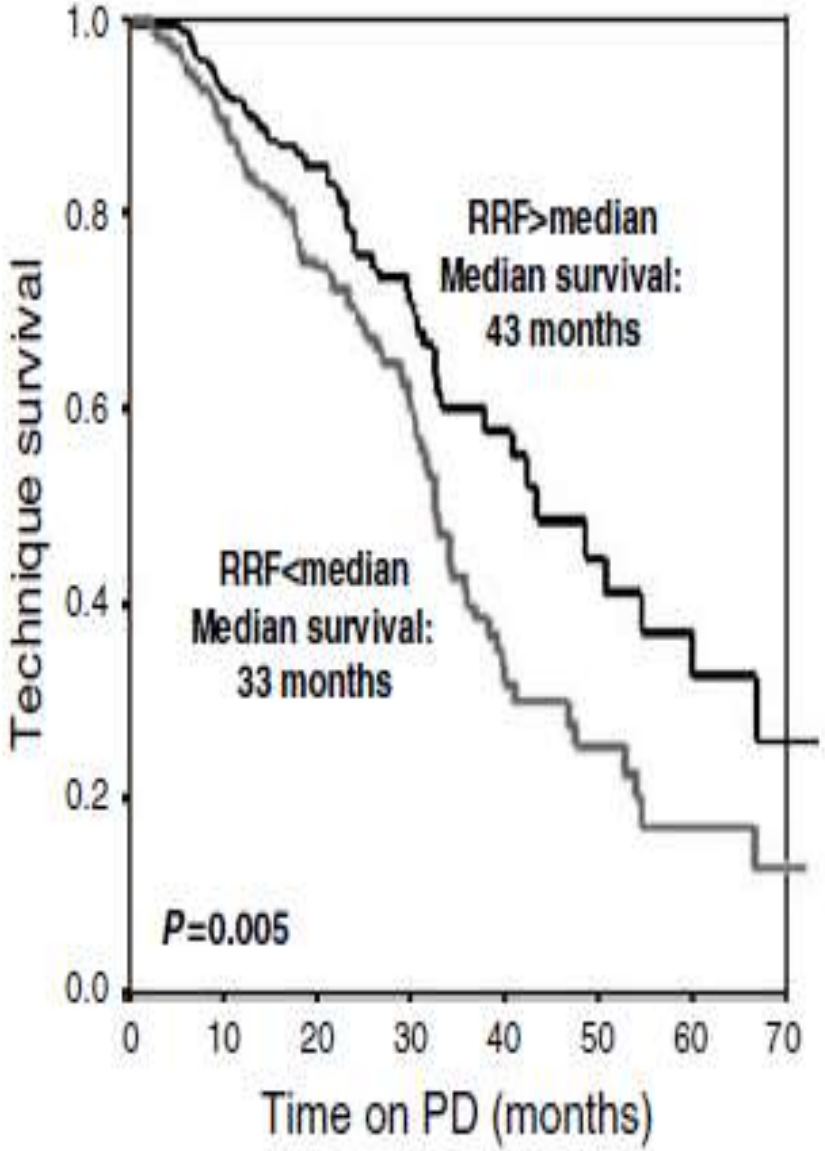


Overall and subgroup analyses of the association of the incremental regimen (vs conventional regimen) with all cause mortality in the matched cohort of 8,419 patients. Points and error bars represent point estimates and 95% confidence intervals, respectively. Abbreviations: HD, hemodialysis; IDWG, interdialytic weight gain; KRU, residual renal urea clearance.

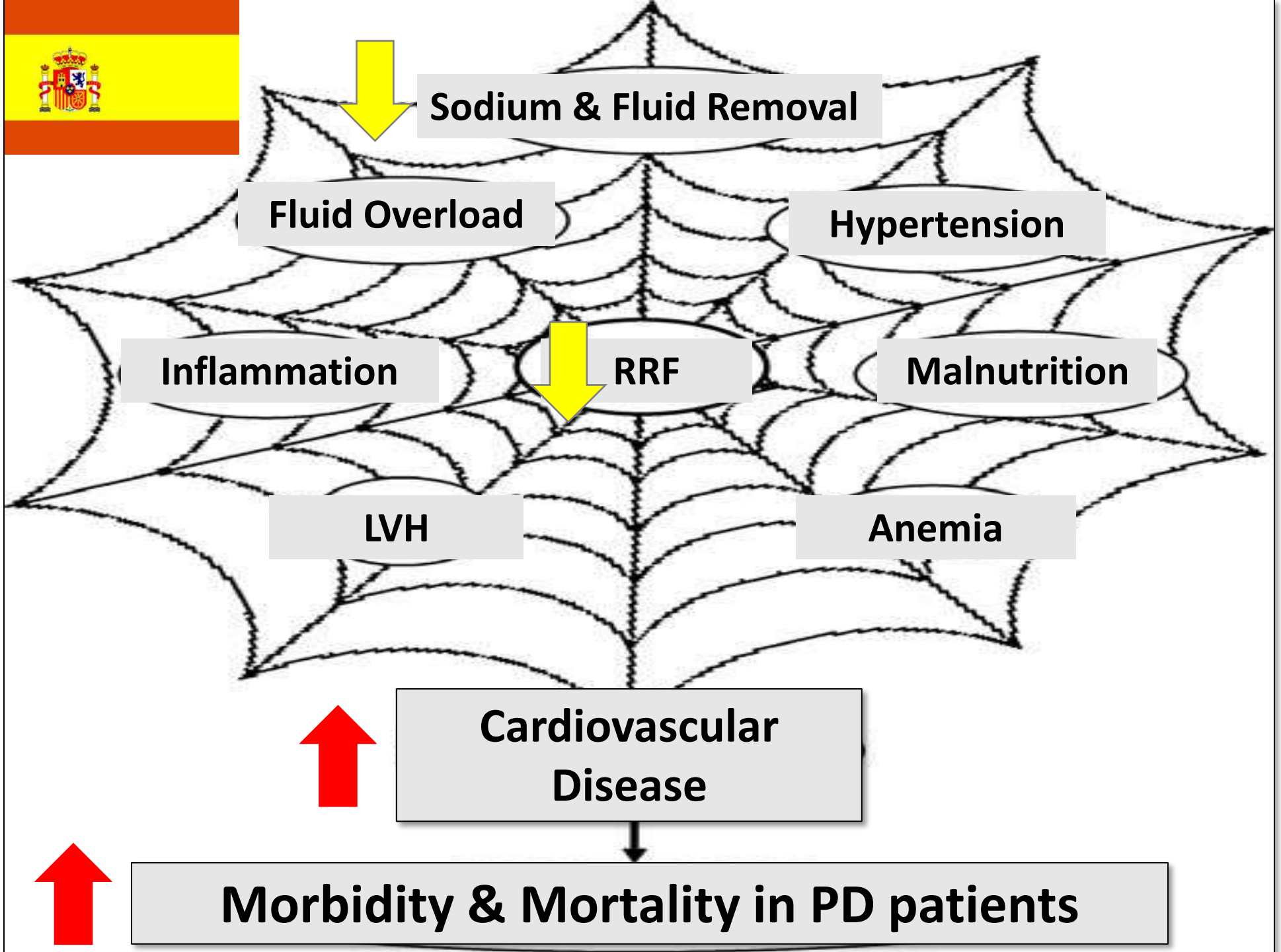


Case-mix–adjusted mortality risk of the incremental hemodialysis regimen among patients in the entire cohort stratified by baseline renal urea clearance (KRU), urine volume, or weekly interdialytic weight gain (IDWG) across the survival periods of 3, 6, 9, and 12 months (M). Points and error bars represent point estimates and 95% confidence intervals, respectively.

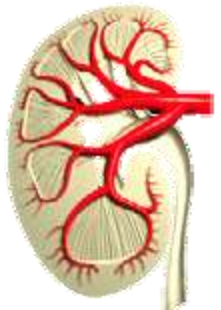




Patient survival and technique success curves, according to RRF from the Andalusian Registry. Technique success refers to the probability of being both alive and on PD therapy.


Sodium & Fluid Removal
Fluid Overload
Hypertension
Inflammation
RRF
Malnutrition
LVH
Anemia
Cardiovascular Disease
Morbidity & Mortality in PD patients

HOW TO PRESERVE RRF



HOW TO PRESERVE RRF

I

Avoid Intradialytic Hypotension

II

Diuretics

(a)Continue diuretics unless urine output is poor.

(b)Loop diuretics increase Na & H2O loss, decreases need for water removal with HD.

(c)Doses up to 160mg/day well tolerated.

HOW TO PRESERVE RRF

III

ACEI & ARB's

Helps preserve RRF.
Effective in PD patients

IV

Aminoglycoside / NSAIDS

Avoid aminoglycosides if possible, nephrotoxic.

V

Iodinated radio contrast media

Nephrotoxic = can lead to ATN & loss of RRF.

HOW TO PRESERVE RRF

VI
Cardiac Disease
Needs to be addressed.
May adversely affect RRF

VII
Hyperuricemia

Conclusion meed chamge

Incremental HD in suitable patients confers many benefits

Decreased CV & all-cause mortality.

Decreased morbidity (> free time).

Economic benefits.

Less problems with vascular access.

Introduction

- most patients with end stage renal disease in the United States are initiated on 3-times per week conventional HD regimen, with little regard to RKF or patient preference.

in 2011 , only China practises incremental dialysis (25%)of incident pts vs all the other 11 countries (<5%) - From DOPPS

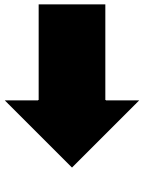
- While RKF has a long history of inclusion into the overall calculation
- of peritoneal dialysis adequacy, it has been largely ignored when
- initiating and prescribing HD
- This may be in part due to the HD urea-based
- “adequacy” targets set forth by the Centers for Medicare and
- Medicaid Services Quality Incentive Program, which do not include
- residual urea clearance (KRU).
- Why now the interest in incremental HD ?

- (While these larger studies provide a more rigorous analytic
- approach,) the observation design has inherent limitations including
- residual confounding by indication and lack of prospective data collection of all important variables.
- A randomized controlled trial has not yet been conducted comparing twice to thrice-weekly HD, and would shed light on the safety and efficacy of incremental HD in select patient populations.

Residual Renal Function

Normal

Glomerular Filtrate = 150L / Day



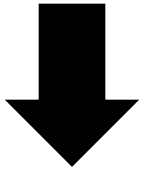
Urine OUTput = 1.5L

Reabsorption = 148.5L

Residual Renal Function

Stage 5 CKD

Glomerular Filtrate = 5L / Day



Urine OUTput = 1.5L

Reabsorption = 3.5L

Why is this so?

Reasons :

I	II	III
Tubular damage	**Volume Expansion**	**Osmotic Diuresis**

Total Renal Function = RRF + RRT

- there are alternative means to
- potentially slow the decline of RKF once HD is initiated, including:
- (1) avoidance of nephrotoxins70,71 (aminoglycosides, nonsteroidal
- anti-inflammatories, radiocontrast dye), (2) control hypertension
- while minimizing intradialytic hypotension,72,73 (3) adjustment of the
- HD prescription (high-flux biocompatible dialyzer membranes and
- ultrapure dialysate water),44,74,75 and (4) possible consideration of a
- low protein diet (0.6-0.8 g/kg/day) on nondialysis days

DEFINITION & HISTORICAL PERSPECTIVES

3. Decline in renal function depends on :

- Aetiology of ESRD
- Treatment modality
- Exposure to nephrotoxic agents
- Cardiac Disease

Candidates for Incremental HD

1. Urine output at initiation of HD is sufficient to keep IDWG < 2kg

2. Serum K^+ and PO_4 is well controlled with diet & PO_4 binders.

3. No history of significant heart failure

4. Good nutritional status.

Look for KZ paper as he has recommendations