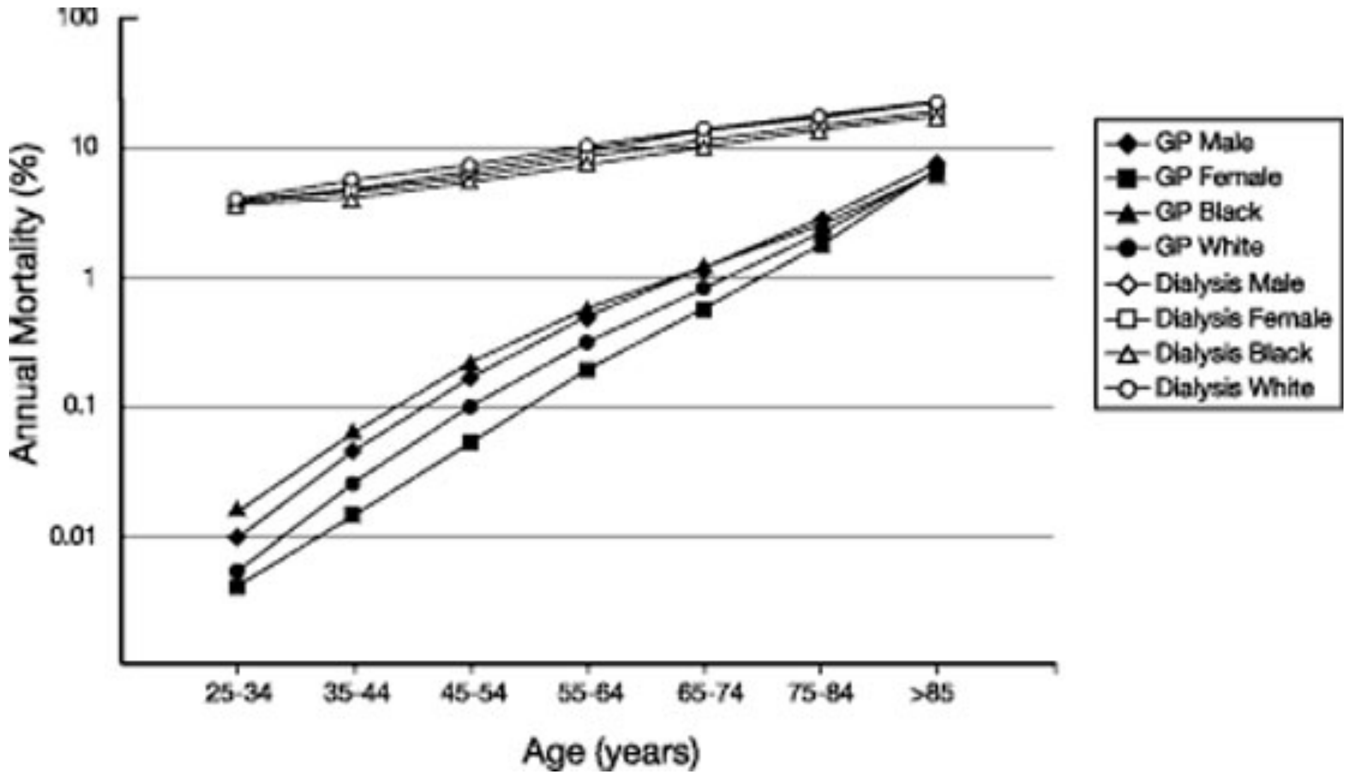
How best to control salt overload in hypertension?

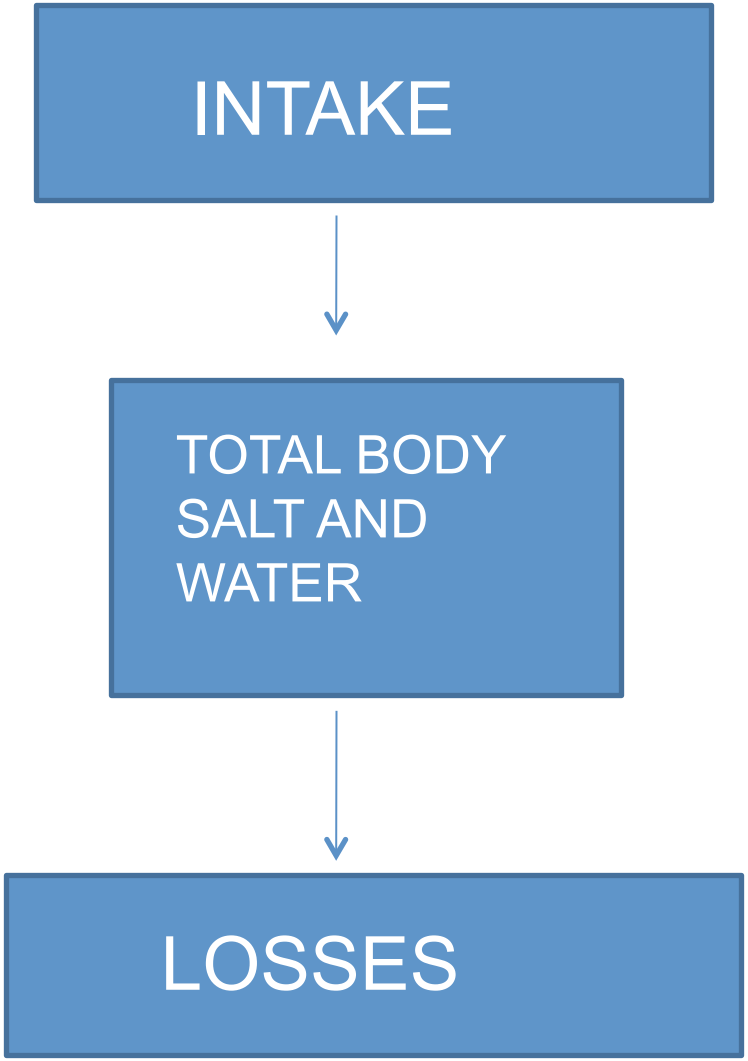
- Dietetic?
- Aligning dialysate sodium with patient's serum sodium

-Prohibition of sodium profiling

Can we control salt and water overload in Haemodialysis patients?

Mortality in Dialysis Patients





Dietary
[Dialysis]

Residual Renal Function
Removal on Dialysis
Other losses

Controlling salt and water overload in HD

- Consequences of salt and water overload
- "Dry Weight"
- Residual Renal Function
- Dietary
  - Restriction
  - Education
- Dialysis
  - Ultrafiltration v Diffusion
  - Dialysate sodium
  - Tools and Toys
    - Blood volume monitoring
    - Dialysate temperature
    - IVC diameter
    - Bioimpedance
    - Natriuretic peptides
  - Time and Frequency

CONCEPT of DRY WEIGHT

Body weight at which composition of body fluid compartments is normal.

At higher weights there is expansion of compartments

At lower weights there is depletion of compartments.

Both these states have adverse clincal consequences.

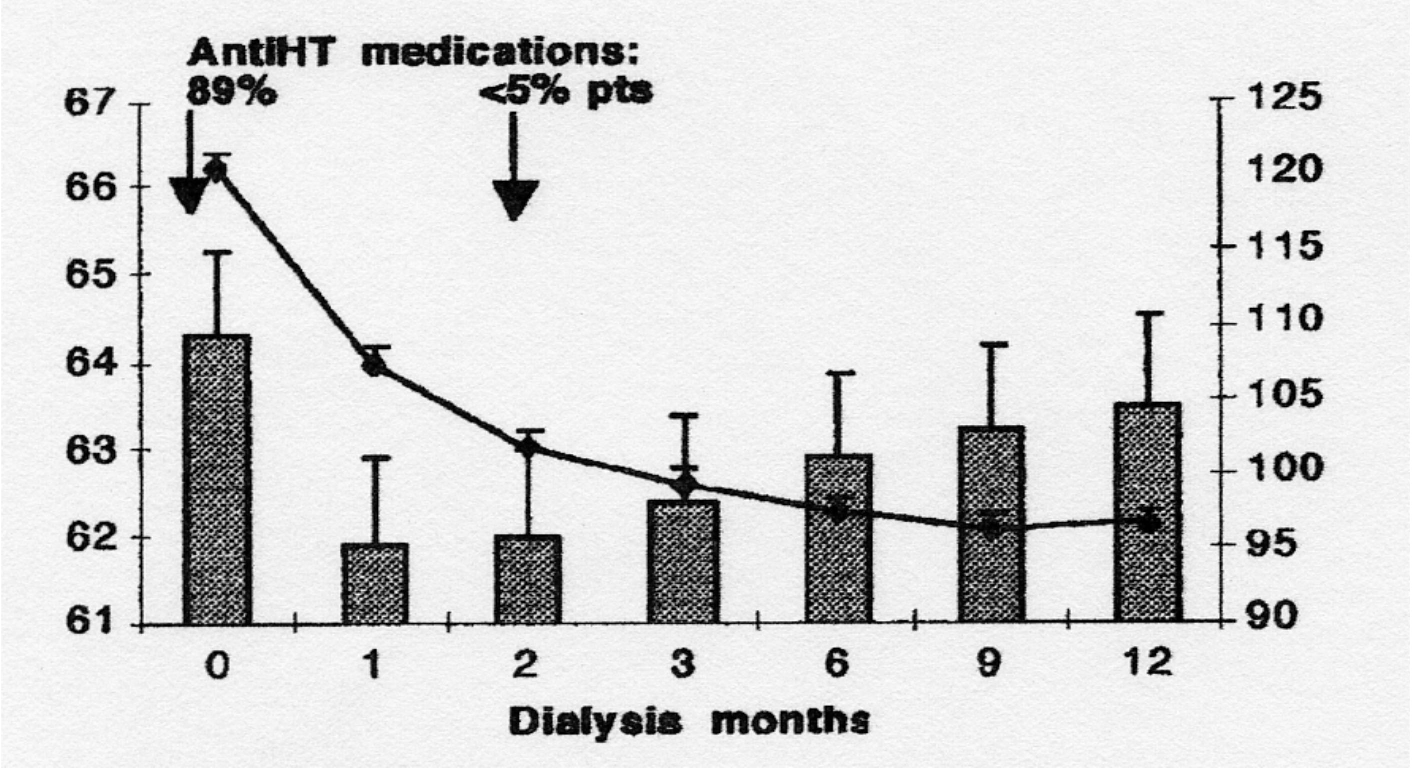
Dry weight

“The lowest [post-dialysis] weight a patient can tolerate without intradialytic symptoms and/or hypotension and in the absence of overt fluid overload” *Henderson KI 17: 571-576; 1980*

“ The post-dialysis weight at which the patient is and remains normotensive until the next dialysis in spite of interdialytic fluid retention and without antihypertensive medication”

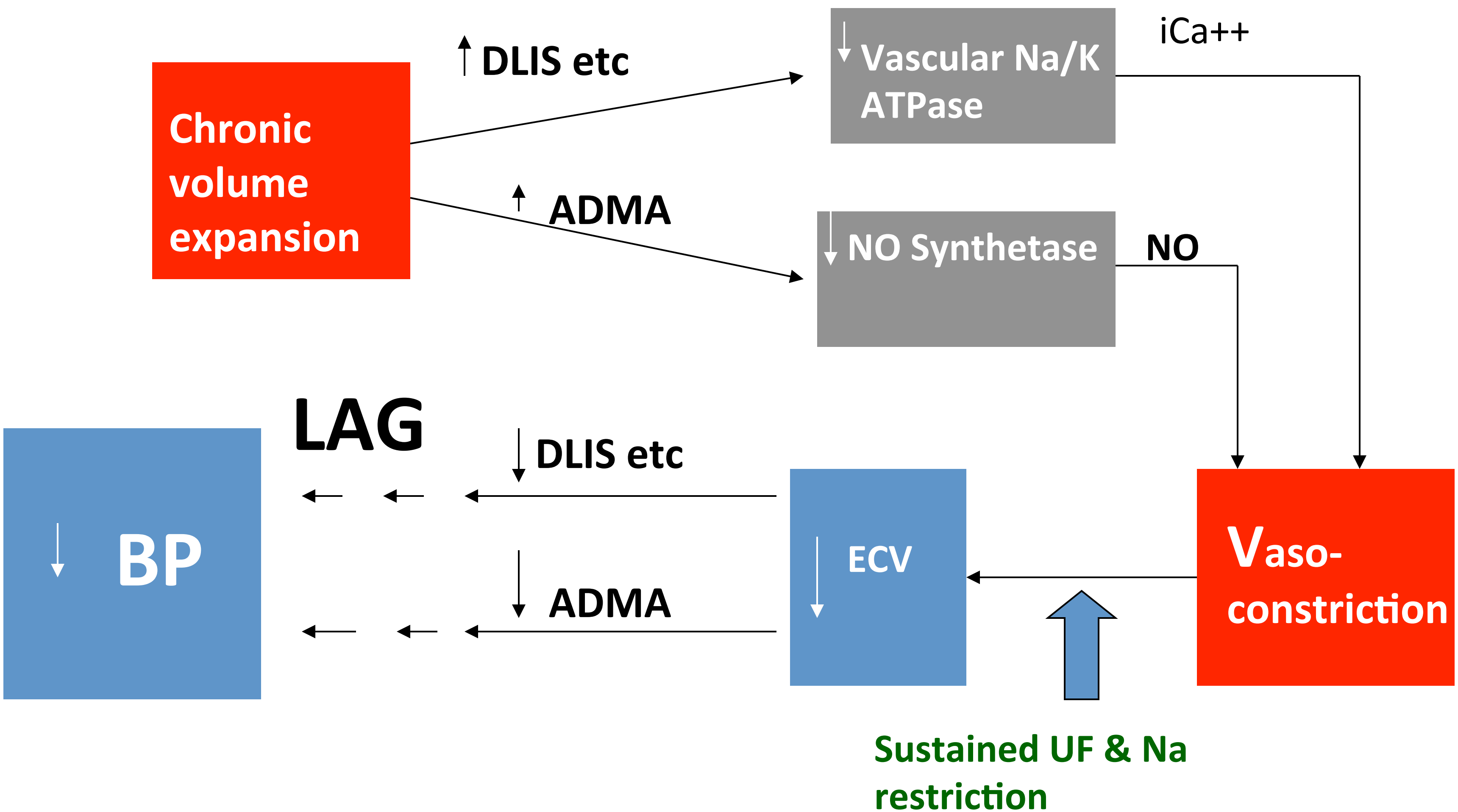
Charra 1996

Probing for dry weight: The lag period



712 patients in Tassin. Charra et al Am J Kidney Dis 32, 720-4, 1998

Lag period between normalisation of ECF and optimal control of BP



Dry weight and Comorbidity

- Cardiac decompensation
- Autonomic dysfunction
- Hypoalbuminaemia
- Hypotensive agents
- Intercurrent illness

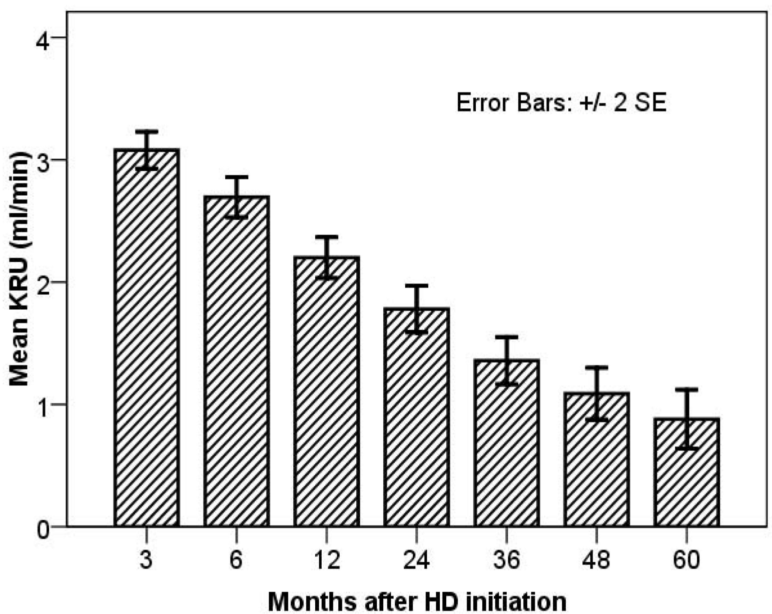
Dry Weight concept: problems

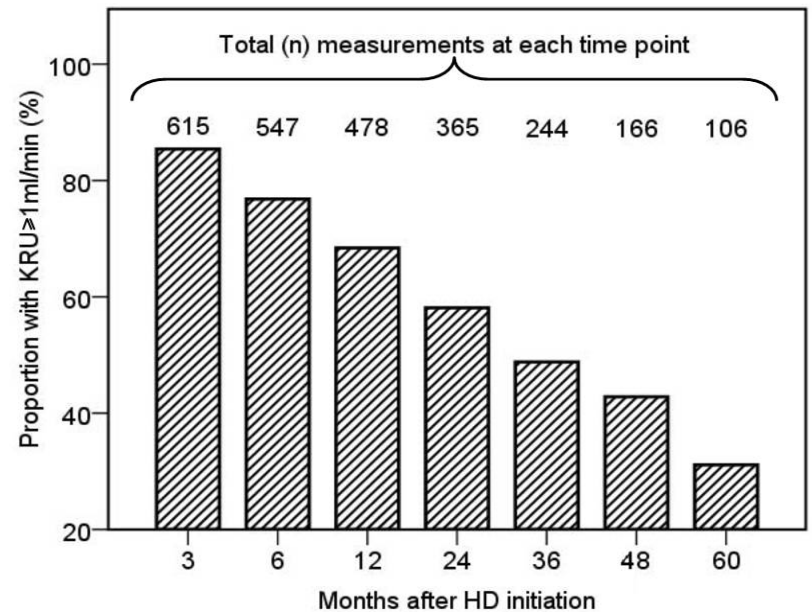
Dry weight ?= best achievable post-dialysis weight

↑ **Defined by trial & error. Iteration over many successive dialysis sessions**

↑ **The best you can manage on the day**

Residual Renal Function in HD

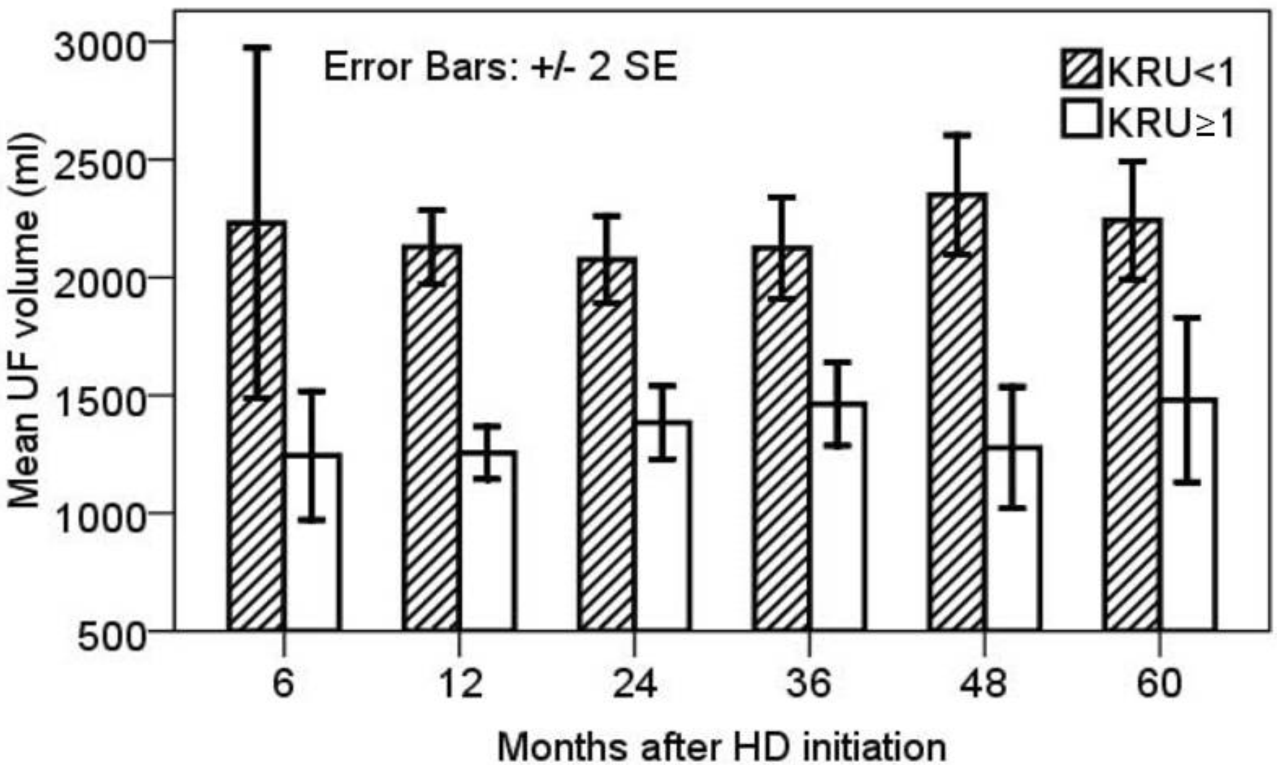




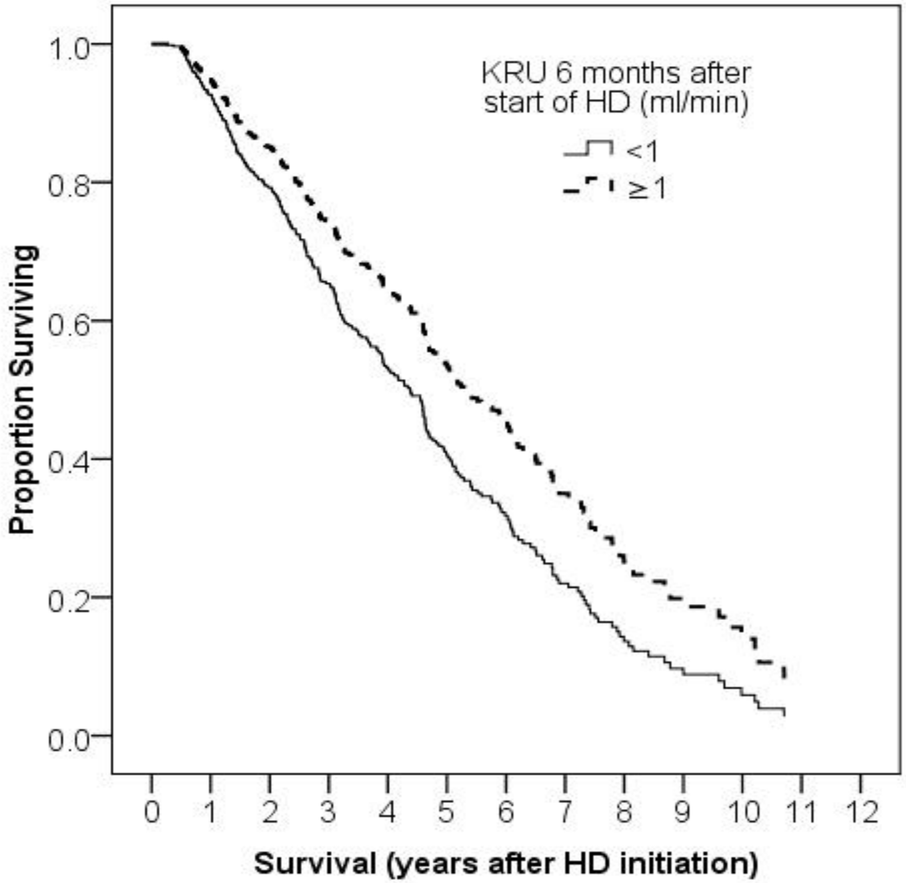
Effects of Residual Renal Function in HD

	6m	12m	24m	36m	48m	60m
Lower K	0.001	0.001	NS	0.005	0.027	NS
Higher Albumin	0.009	0.017	0.034	0.005	NS	NS
Higher nPCR	<0.001	<0.001	0.002	0.019	NS	NS
Lower EPO dose	NS	<0.001	0.003	<0.001	0.005	NS
Lower ERI	NS	<0.001	0.004	0.003	0.005	NS
Lower Phosphate	NS	NS	NS	NS	0.048	NS

Residual Renal Function and UF Volume



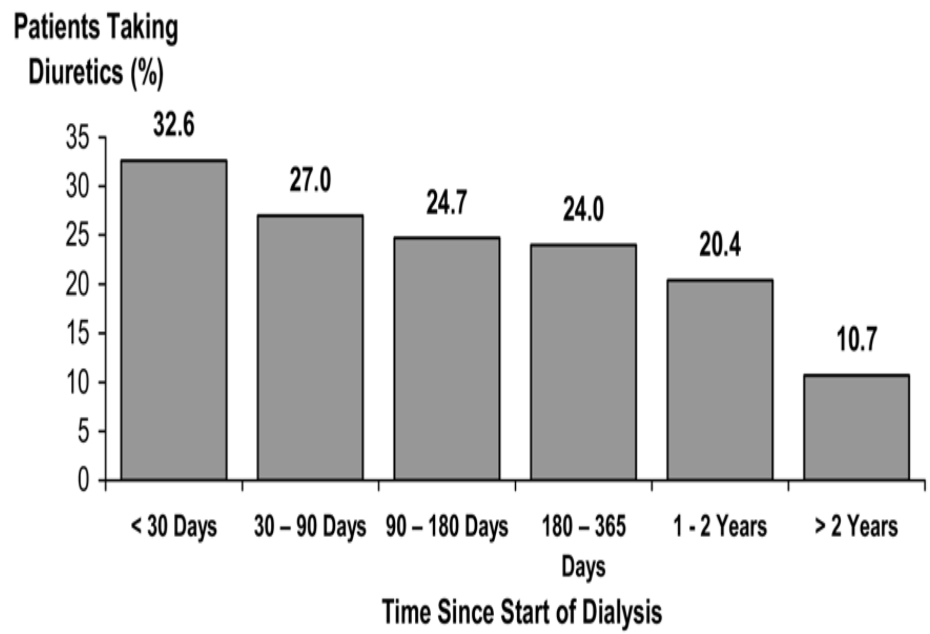
Residual Renal Function and Survival



	Sig (p)	*Hazard ratio*
KRU_{BSA} ^{TIME}	0.029	0.932
Diabetic status	0.200	1.272
Age	<0.001	1.030
Albumin	0.003	0.962
HDF use	<0.001	0.508
Malignancy	0.001	1.841
Ischaemic heart disease	0.589	0.925
Peripheral vascular disease	0.684	1.070

Diuretic use associated with:

- Less interdialytic weight gain
- Reduced hyperkalaemia
- Reduced intradialytic hypotension
- Better preservation of residual renal function
- Lower relative risk of cardiac death
- Trend to a reduced risk of all-cause mortality



Bragg-Gresham JL *et al. (2007) Diuretic use,* residual renal function, and mortality among hemodialysis patients in the Dialysis Outcomes and Practice Pattern Study (DOPPS). *Am J Kidney Dis* ***49: 426–431***

Is there a conflict between achievement of dry weight and maintenance of residual renal function?

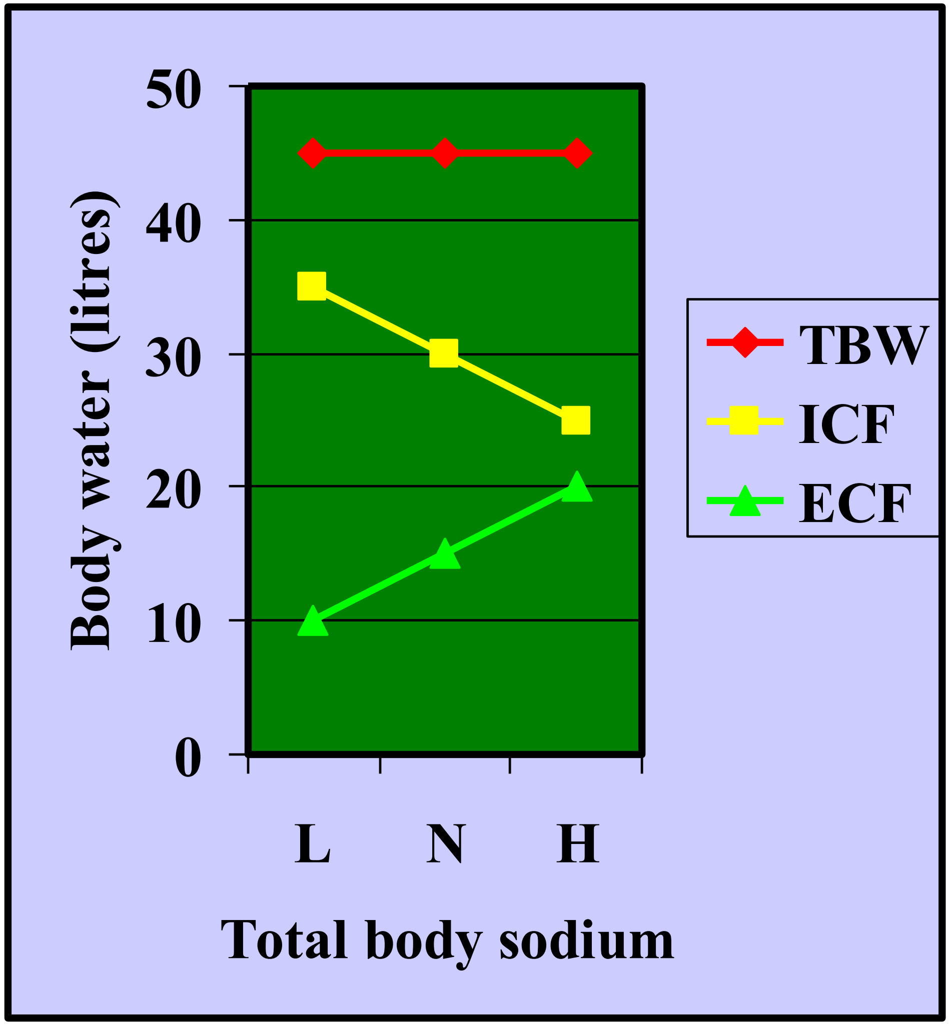
	Baseline	Following drug treatment	Following volume control	P<
Weight (kg)	61 ± 6	60 ± 5	55 ± 8	0.0001
Systolic BP (mmHg)	175 ± 15	138 ± 11	125 ± 9	0.0001
Diastolic BP (mmHg)	99 ± 11	77 ± 10	71 ± 8	0.0001
Urine volume (mL/day)	1575 ± 281	1393 ± 275	40 ± 47	0.0001
Cardiothoracic Index (%)	0.57 ± 0.05	0.55 ± 0.06	0.46 ± 0.03	0.0001
LVMI (gr/m^2)	265 ± 63	251 ± 59	161 ± 25	0.0001
Ejection fraction (%)	56 ± 6	59 ± 6.5	67 ± 4	0.0001

Gunal et al Should the Preservation of Residual Renal Function Cost Volume Overload and Its Consequence Left Ventricular Hypertrophy in New Hemodialysis Patients? Renal Failure 2004

Total body sodium and water

Water = weight,

Salt = thirst and ECF expansion & hypertension



Sodium versus sodium-fluid restriction in hemodialysis

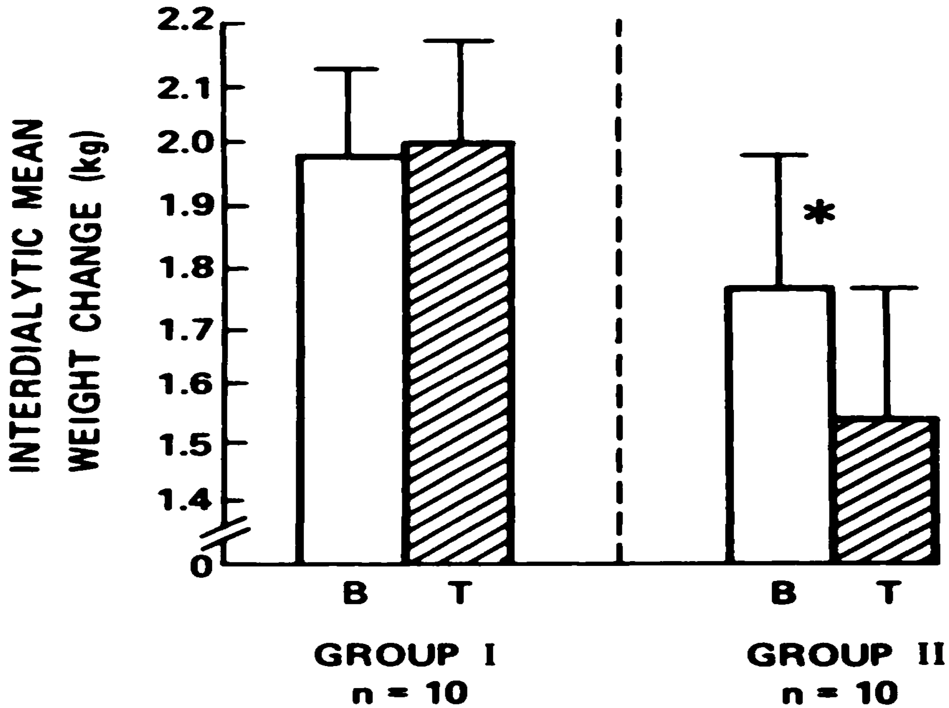


FIG. 1. Mean interdialytic weight gains in kilogram. Group I received sodium-fluid diet instruction. Group II received sodium restriction only. Asterisk represents a significant difference ($P < 0.05$) between base-line (B) and treatment (T) measurements.

Rupp et al. Am J Clin Nutr. 1978

Salt restriction v [Salt] + Water Restriction

- During one interdialytic period, patients were placed on a very restricted 1 g sodium diet but were told not to limit fluid intake and to drink when thirsty.

- During the control interdialytic period, patients were told to follow their usual salt and water restrictions.

- IDWG was significantly lower during the restricted salt/unrestricted water intake period than during the control period (1.9 ± 0.2 v 2.8 ± 0.2 kg).

Rigby-Matthews et al. JASN 1999, 267A

RCT of Patient Education

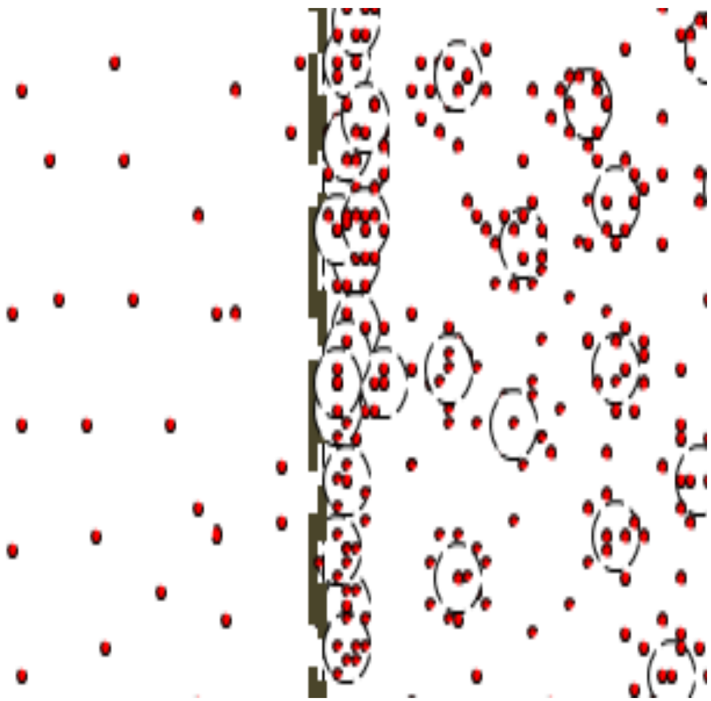
- Pre-dialysis education
  - 5 RCTs – none reporting the effects on salt and water management
- On-going education on HD
  - 22 RCTs
  - 6 RCTs addressing "fluid restriction" – 4 showing a significant short-medium term reduction in IDWG

Diffusion vs Convection

- Most sodium loss during dialysis occurs by UF
- The sodium content of the ultrafiltrate is very similar to that of plasma

Diffusion vs Convection

Gibbs-Donnan Effect



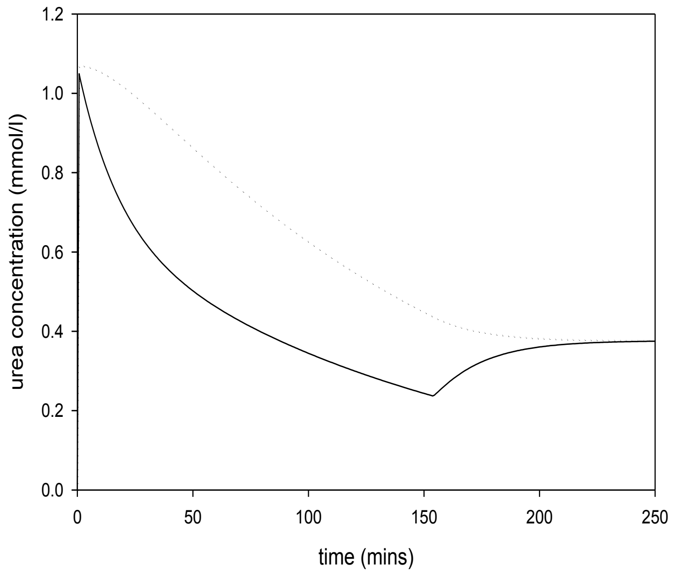
Dialysate **Blood**

- UF produces an hypotonic dialysate – uncoupling sodium and water removal
- Patients are sodium overloaded in direct proportion to UF volume
- Achieving sodium balance requires EXCESSIVE UF OR DIFFUSIVE SODIUM LOSS

Flanigan KI 2000

Dialysis fluid sodium

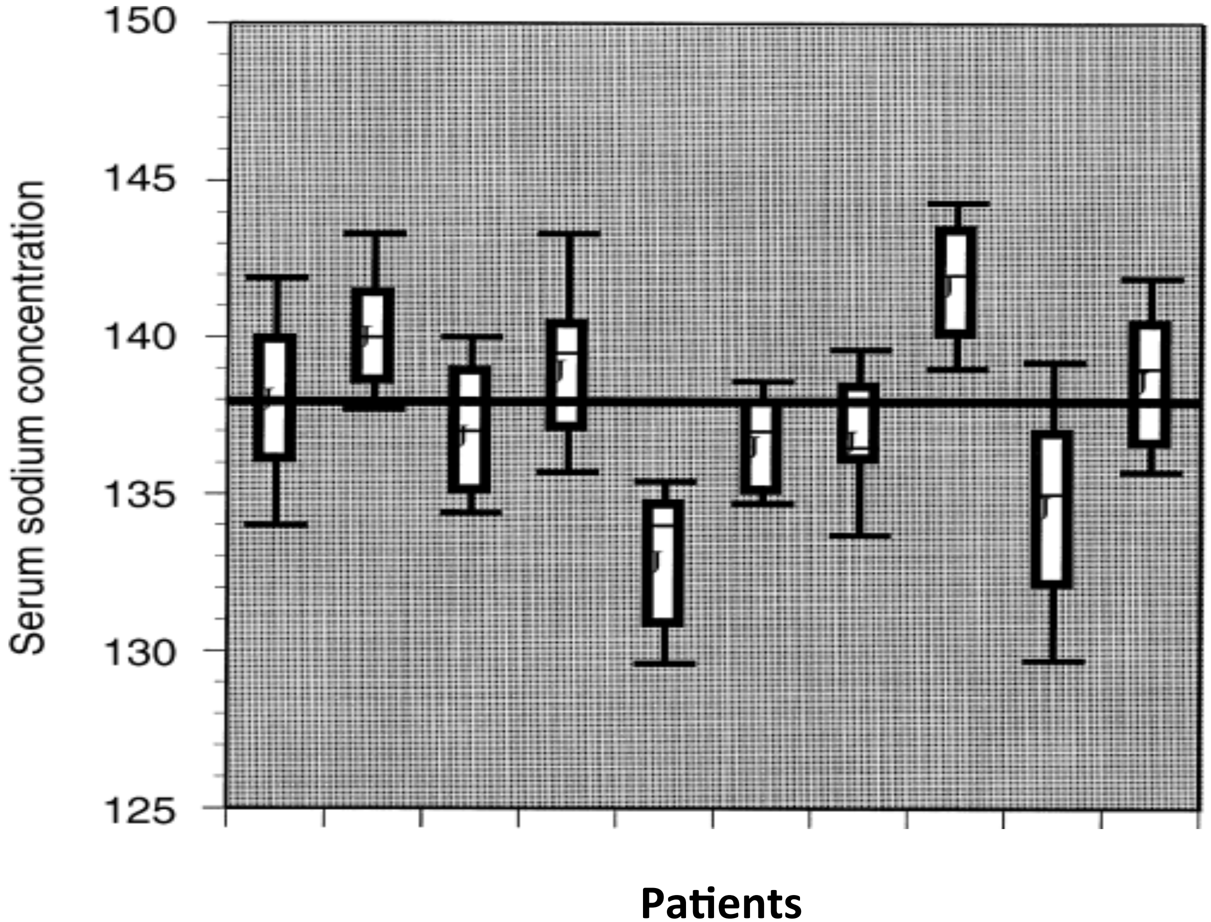
	Plus	Minus
130	Less weight-gain, thirst , hypertension	More hypotension & headache
140	Less hypotension headache	More weight gain, thirst & hypertension



Sodium: What you see is………
…………….. not what you get?

- Gibbs-Donnan phenomenon
- $[Na^+]_{plasma\ water} > [Na^+]_{plasma}$
- Non-ideal behaviour
  - $a_{Na^+} = f\,[Na^+]$
- Measurement techniques
  - Flame photometer v ion-selective electrode

What is a high dialysate sodium?



Individual osmolar "set point"

Flanigan 2000

Dialysis Fluid

- Isotonicity can only be defined for the individual
- For isonatraemic dialysis [zero diffusive sodium removal]

$$[Na^+]_{plasma} = [Na^+]_{dialysate}$$

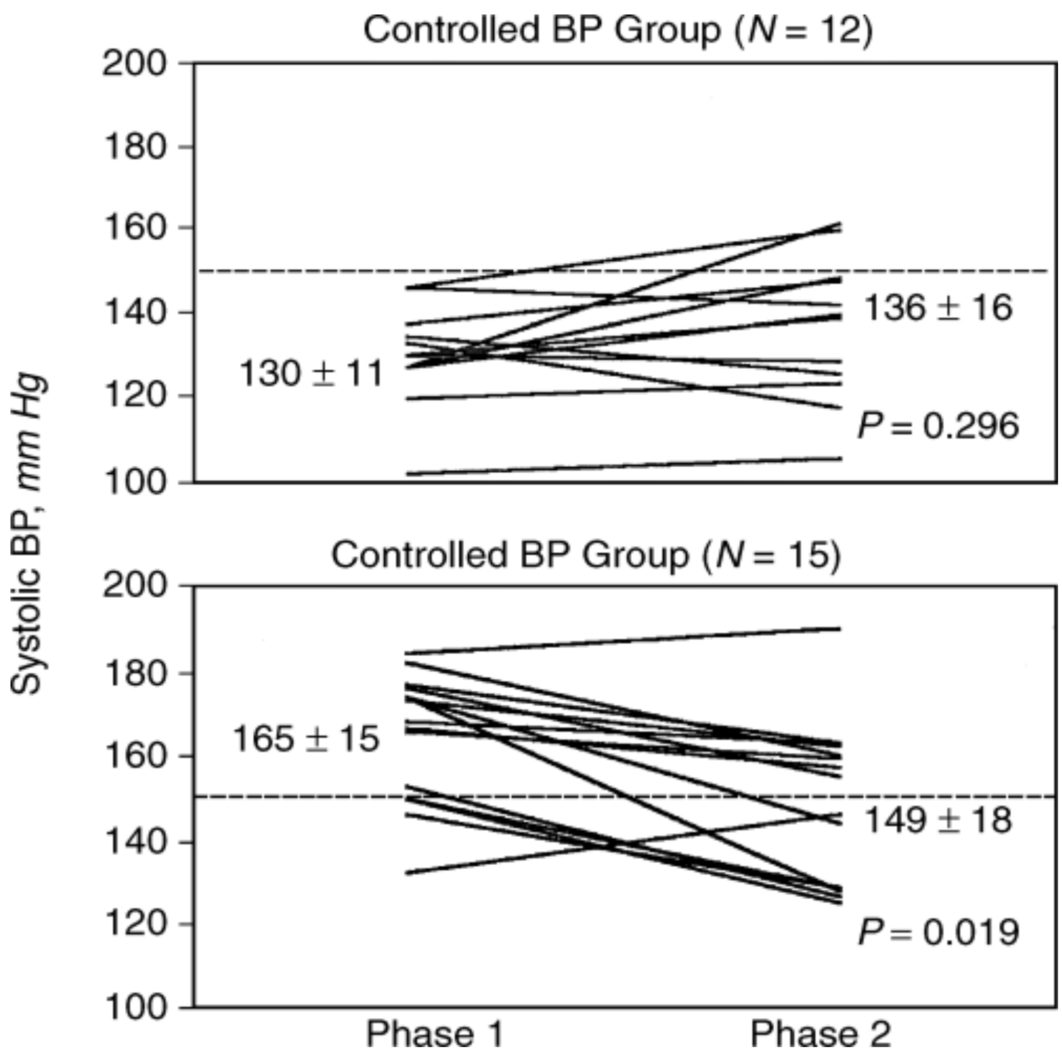
The importance of dialysate sodium concentration in determining interdialytic weight gains in chronic hemodialysis patients: The PanThames Renal Audit.

2187 patients: Dialysate Na^+ >140 v 136 mmol/l

- Mean interdialytic weight gain 4.1% v 2.8% ($p<0.05$).
- Mean pulse pressure 70 vs 63 mmHg ($p<0.011$).
- Symptomatic hypotension 13.5% v 2.7% ($p<0.05$).

Davenport et al. Int J Artif Organs 2008

Clinical consequences of an individualized dialysate sodium prescription in hemodialysis patients



27 patients

Pre –HD [Na^+] x 0.95 =
Dialysis fluid [Na^+]
(ion-selective electrode)
Versus
Standard [Na^+] =138 mmol/l

Less weight gain, thirst and Intradialytic hypotension in the individualized Na^+ period compared with standard phase.

De Paula et al. KI 2004

Sodium Profiling

HIGH to LOW

Early sodium influx counteracts fall in plasma osmolality due to urea disequilibrium

Aids UF by maintaining refill

In latter stages diffusive sodium loss

Studies on profiling

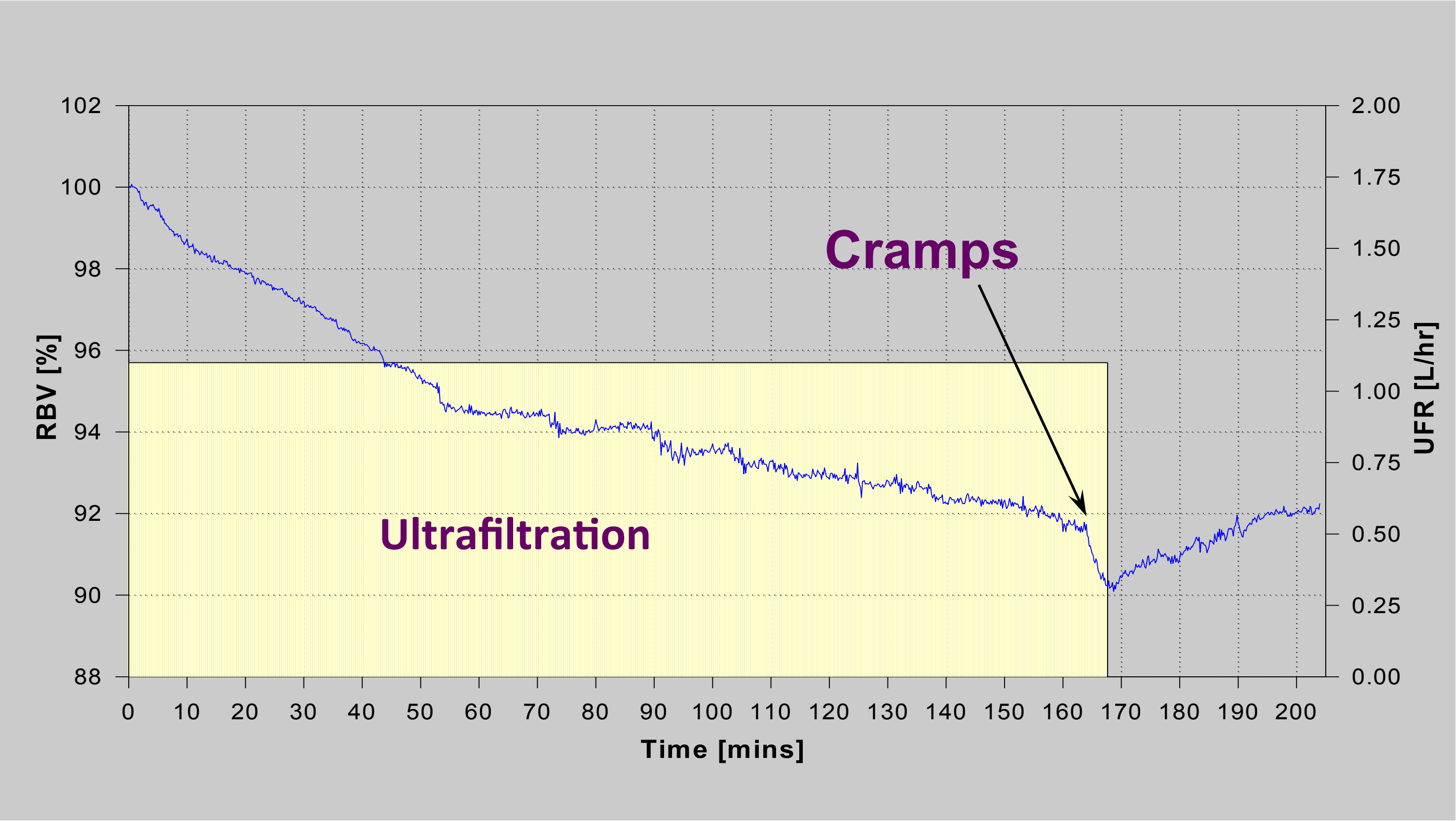
30 Studies

- Small heterogeneous groups
- Brief
- Wide variety of profiles
    - 90% high-to-low
- Inappropriate comparisons, majority of profiles add sodium by diffusion (high time average dialysate sodium concentration)
    - 60% adding sodium by diffusion
    - 23% “isonatraemic”
    - 17% “individualized”

Outcome of Sodium Profiling Studies

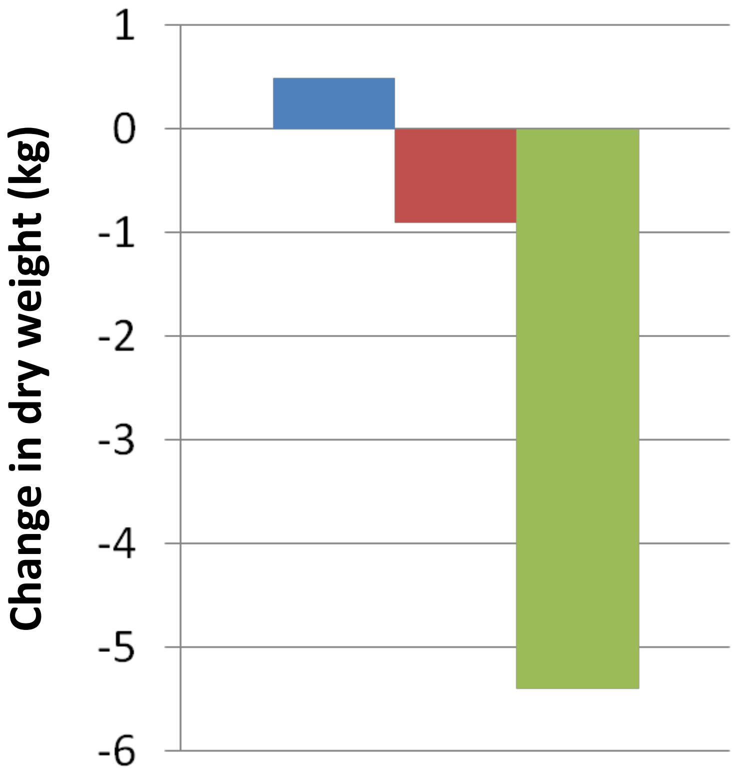
	LESS HYPOTENSION	LESS DISEQUILIBRIUM	SODIUM RETENTION
Positive	14/18	10/18	11/18
Neutral	4/7	1/7	?
Individualised	5/5	3/5	?

On-line RBV profile (continuous UF)



Clinical Utility of BVM

BV reduction (%)	**16**	**12**	**6**
Post HD refill	**-**	**+**	**-**

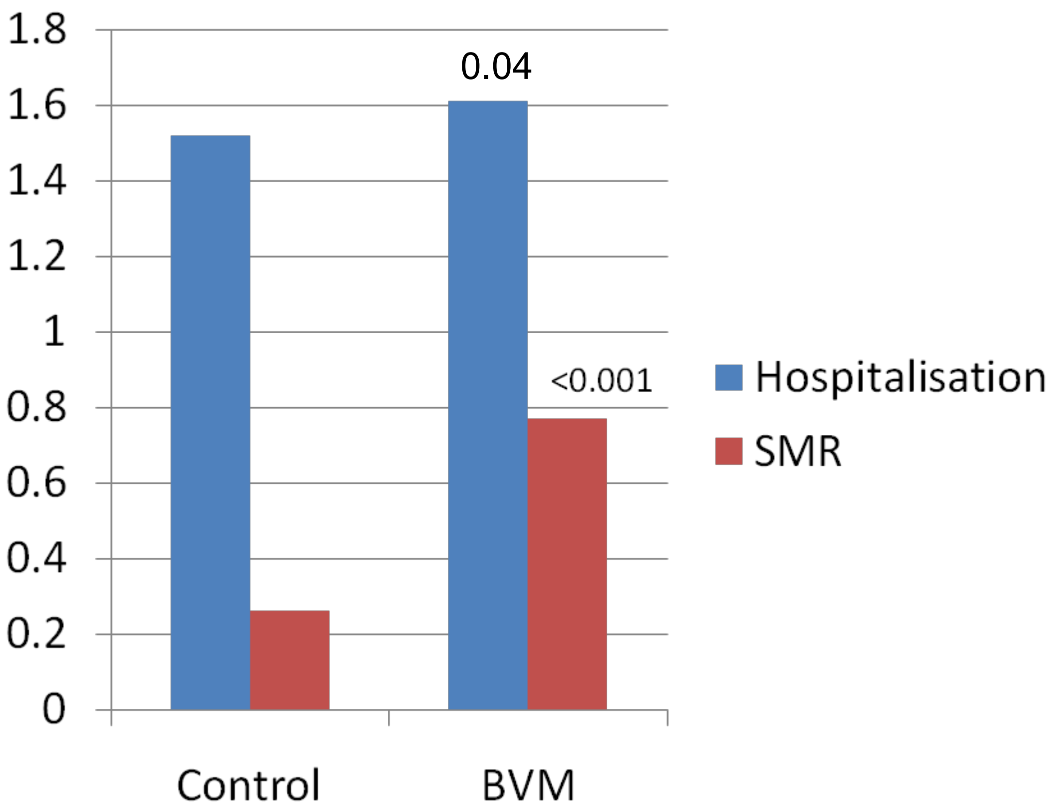


28 patients

- Reductions in dry weight
- Reduction in hospitalisations for fluid overload

Rodriguez et al 2005

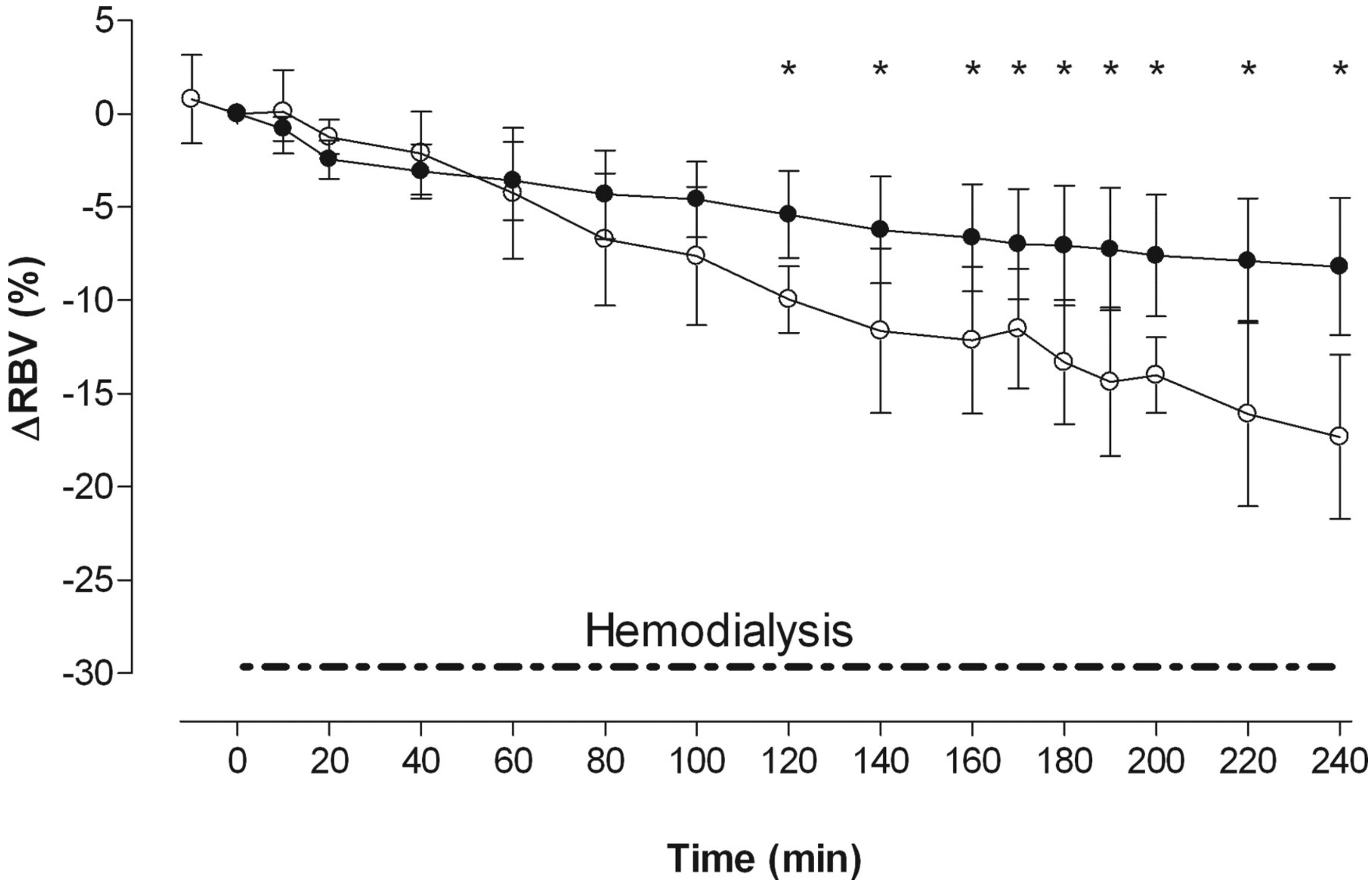
RCT: BVM v conventional monitoring



227 patients BVM v 216 Conventional monitoring

Reddan et al: JASN 2005

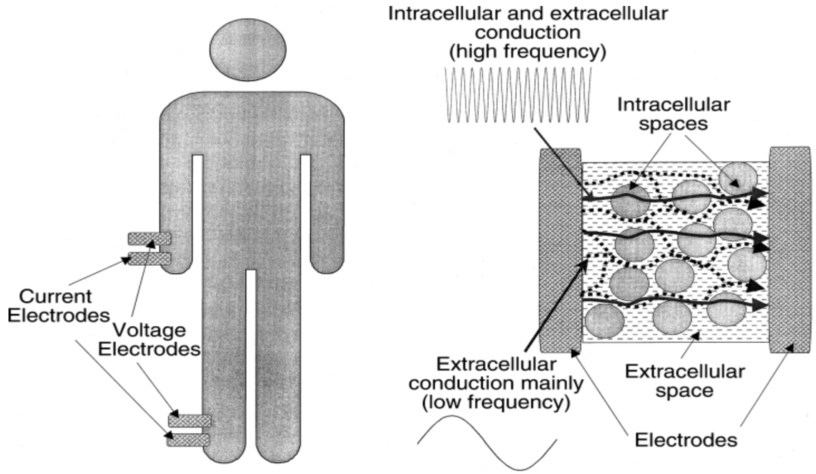
The mean course of total blood volume changes ΔTBV (circle) and relative blood volume changes (ΔRBV; filled circle) during (HD) in seven patients

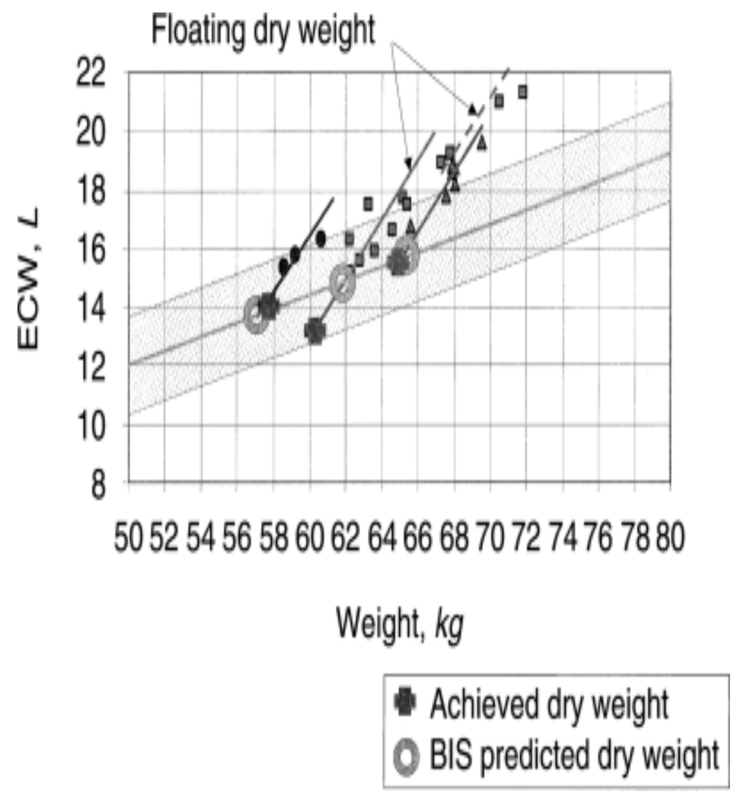


Dasselaar, J. J. et al. Clin J Am Soc Nephrol 2007;2:669-674

CJASN

MULTI-FREQUENCY Whole body bioimpedance

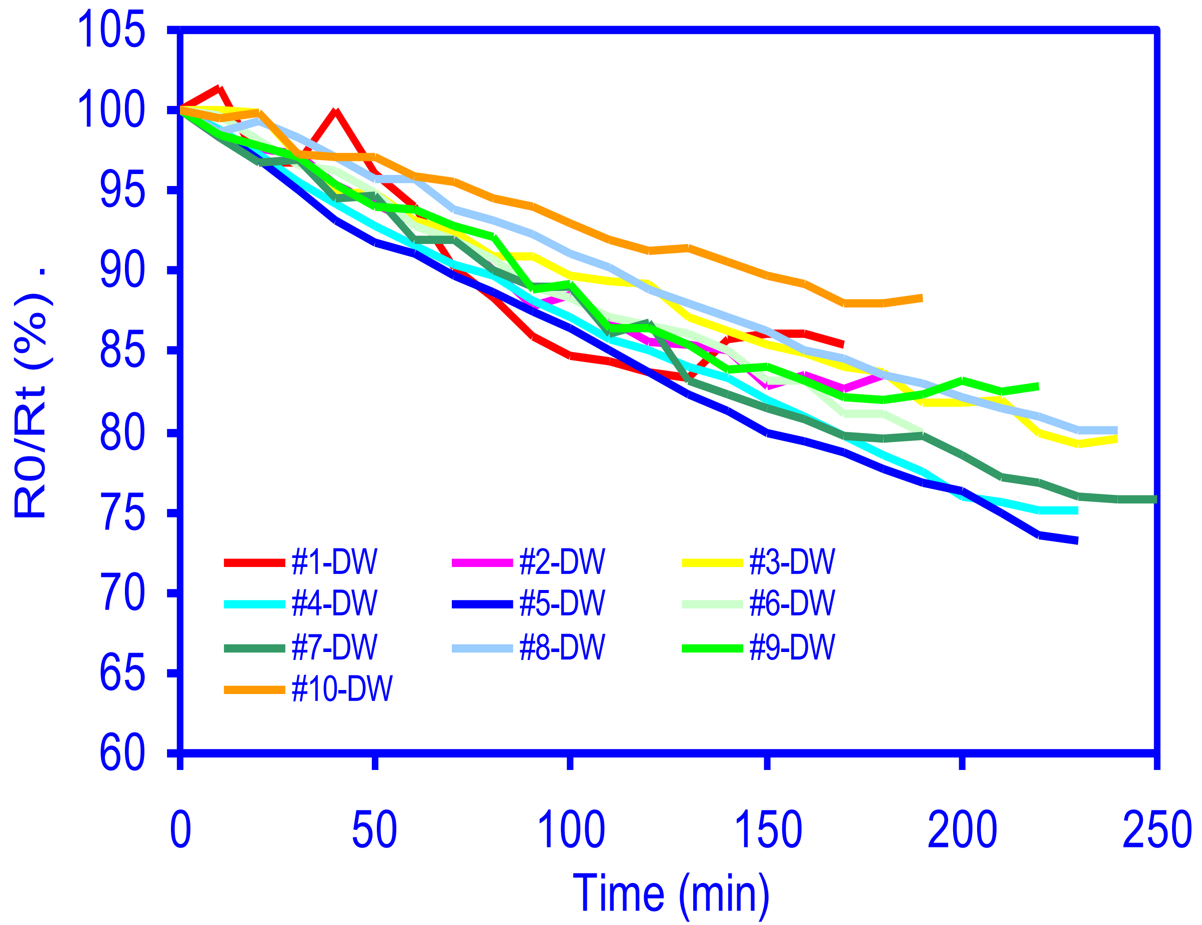




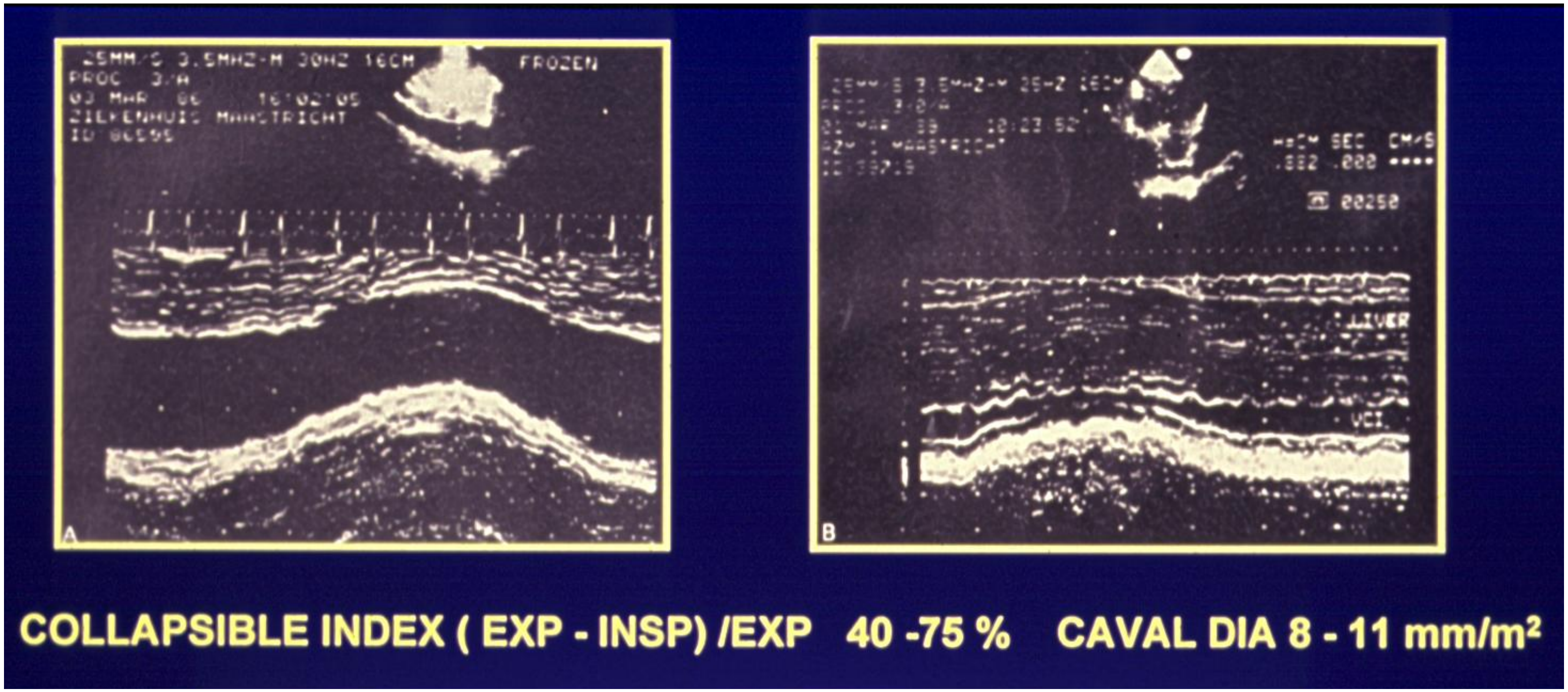
Problems –
1.Fluid distribution in trunk
2.What's normal in HD patients?

Chamney et al KI 2002

Continuous segmental bioimpedance: Intradialytic Relative Resistance in Leg



INFERIOR VENA CAVAL DIAMETER



Overhydration: VCD > 11, CI < 40%

Ideally measured 2hrs post dialysis

Limitations: Operator variability, heart failure

Natriuretic peptides and the dialysis patient

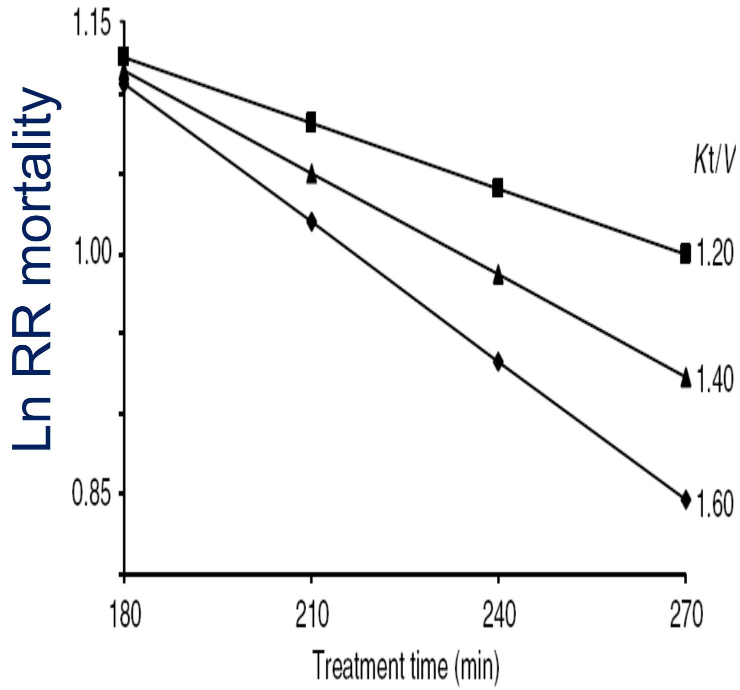
BNP correlates well with cardiac function, and is a good prognosticator for risk stratification

ANP is sensitive to volume changes during dialysis, but changes in concentration do not predict achievement of euvolemia.

Suresh et al. Seminars in Dialysis 2005

Effect of treatment time

Saran et al (DOPPS), KI 69:1222-28, 2006



UFR>10 ml/h/kg independently associated with:

➢higher odds of intradialytic hypotension (odds ratio =1.30; p = 0.045)

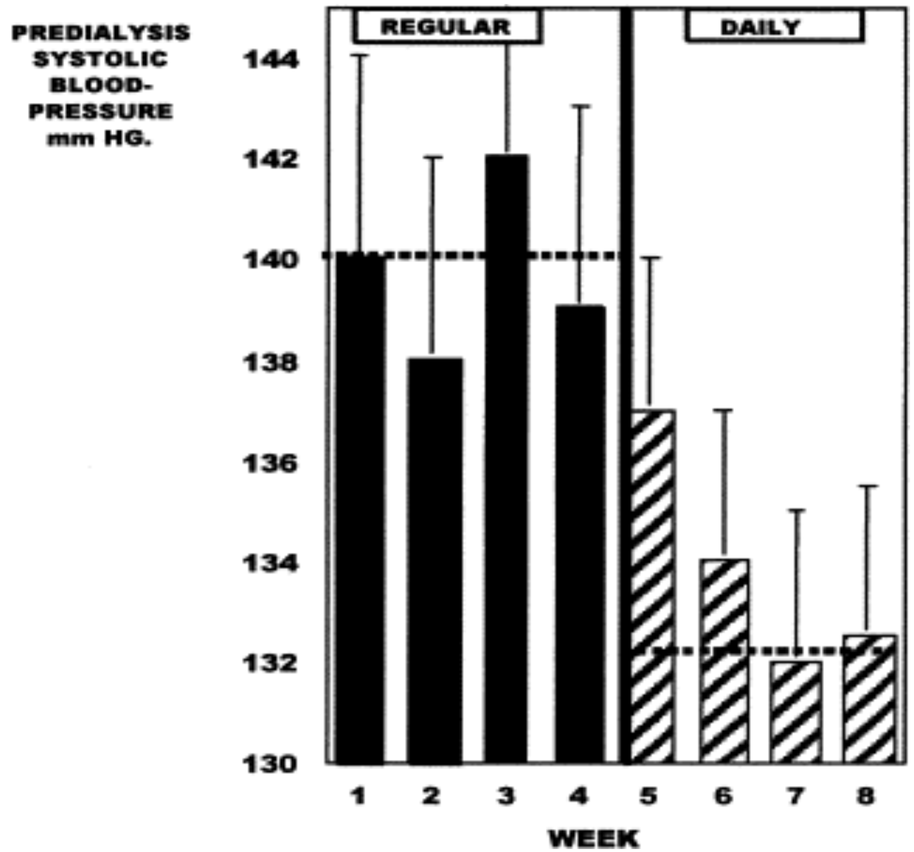
➢higher risk of mortality (RR = 1.09; p = 0.02).

BP following switch from thrice –weekly to quotidien HD

UF volume on standard HD 3.2 ± 1.3 kg (9.6 kg/wk) v 1.9 ± 0.9 kg (11.4 kg/wk) during daily dialysis (*P* < 0.0001).

Weight loss/hr less on standard dialysis (0.81 ± 0.32 versus 0.95 ± 0.49 kg; *P* < 0.0001).

No difference in mean post-dialysis weights.

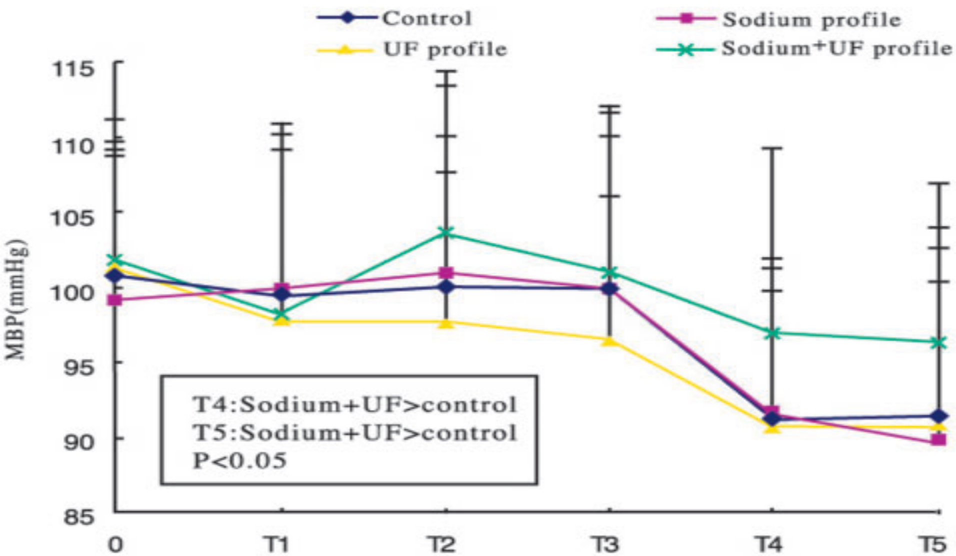


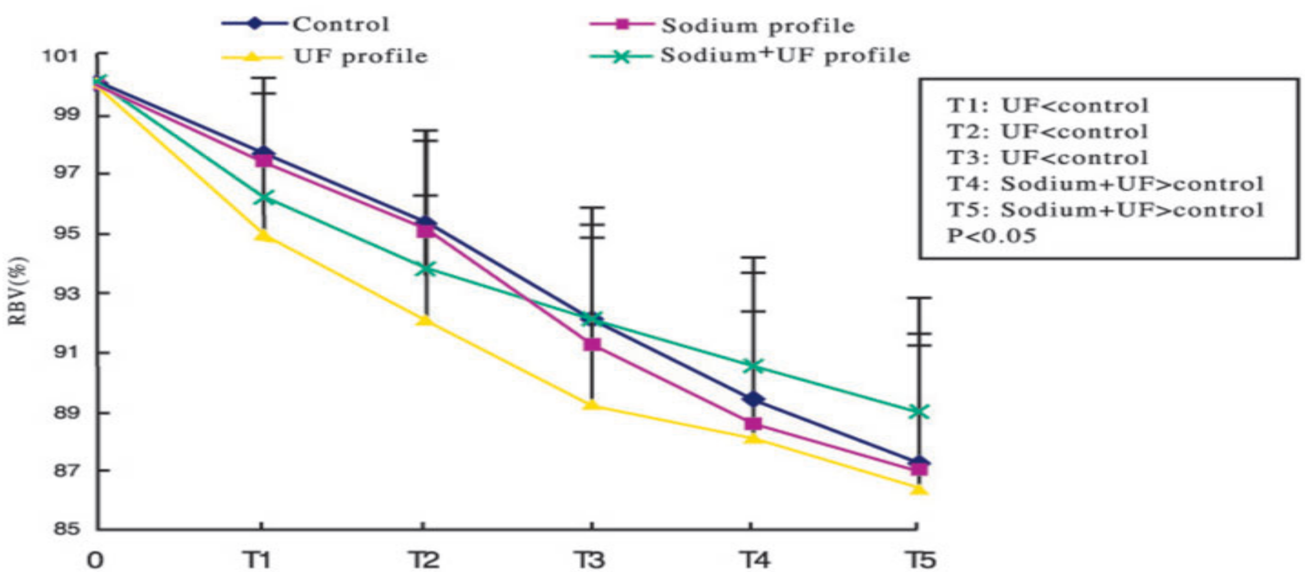
Williams et al: AJKD 2004

Main Points

- Efforts should be made to conserve residual renal function though not at the expense salt and water overload
- Importance of sodium restriction is underestimated
- We should use dialysate sodium concentration more intelligently
- We need to be clear what we are measuring and how
- In the absence of residual renal function – dialysis time/frequency are the main backstops
- The role of most “tools and toys” still ill-defined. At best most are an adjunct to clinical judgement
- Does the dry weight concept work for patients with significant cardiac dysfunction, autonomic dysfunction, and other comorbidities?

Zhou et al NDT 2006





Time during HD session

With the similar intradialytic sodium removal, during sodium balance-neutral linearly decreasing sodium profile combined with linearly decreasing UF profile

-Better preservation of blood volume

- Less hypotensive episodes

Biofeedback techniques

Blood volume

Blood Volume Reduction controlled by varying UF rate and dialysis conductivity. Basile et al; NDT 2001. Santoro et al KI, 2002

Thermal balance

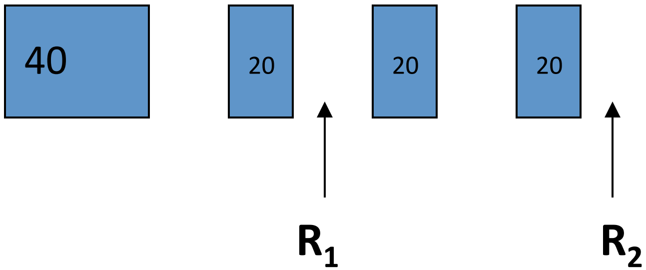
Maggiore et al; AJKD 2002. Santoro et al; NDT 2002

Arterial pressure

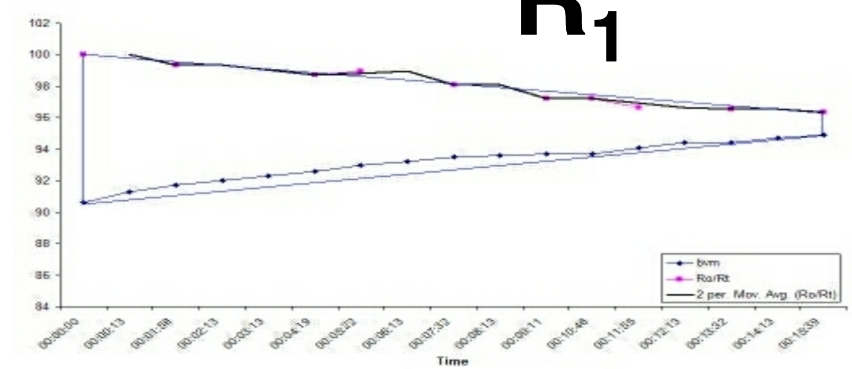
Arterial pressure controlled by varying UF rate. Mancini et al NDT; 2003.

Combined continuous segmental bio impedance and relative blood volume (RBV) monitoring.

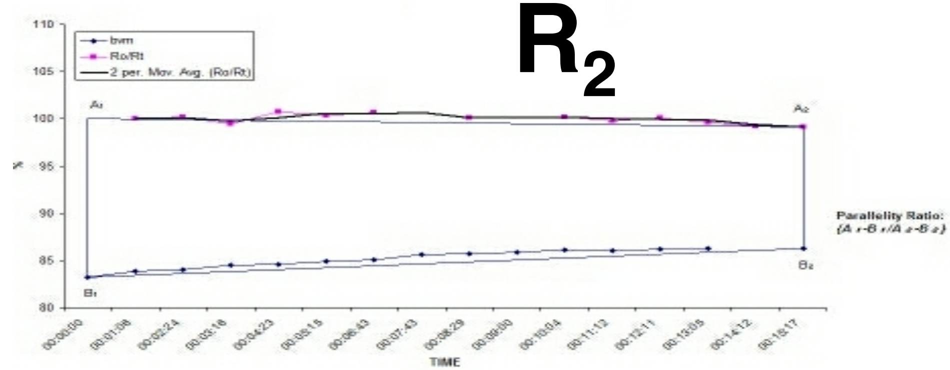
UF pulses



R1



R2



In R_1, the RBV trace and the ECF relative resistance trace converged, RBV rising and ECF relative resistance continuing to fall) reflecting adequate refill.

In R_2 , both RBV and ECF relative resistance traces plateaued, and the traces tended towards parallel. reflecting critically reduced refill.

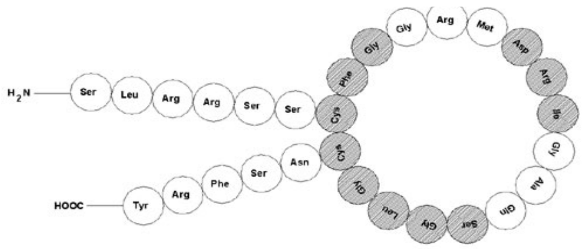
PROFILED DIALYSIS

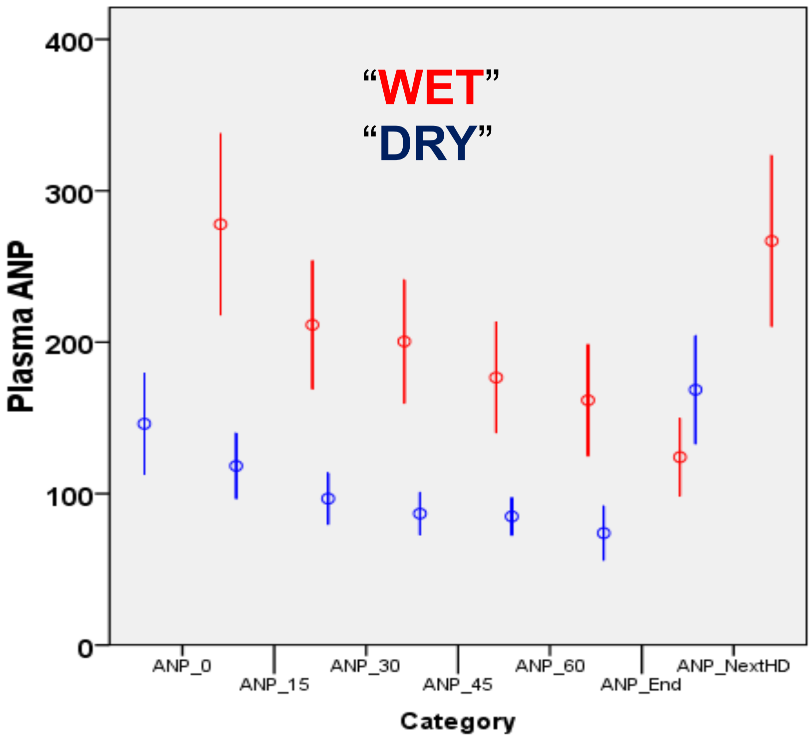
Dialysate Sodium

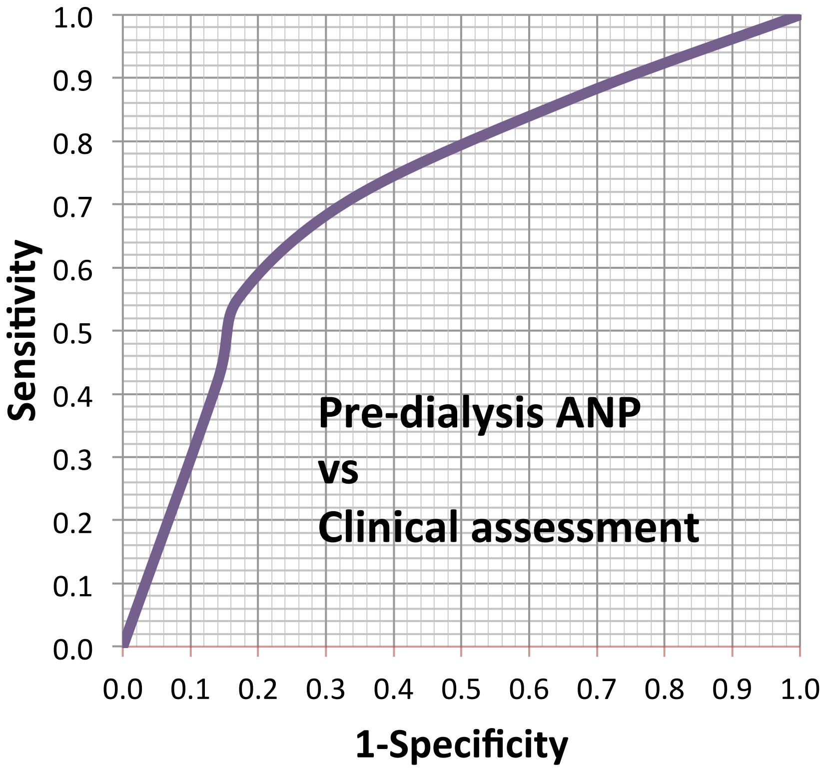
Ultrafiltration Rate

Natriuretic Peptides in HD patients

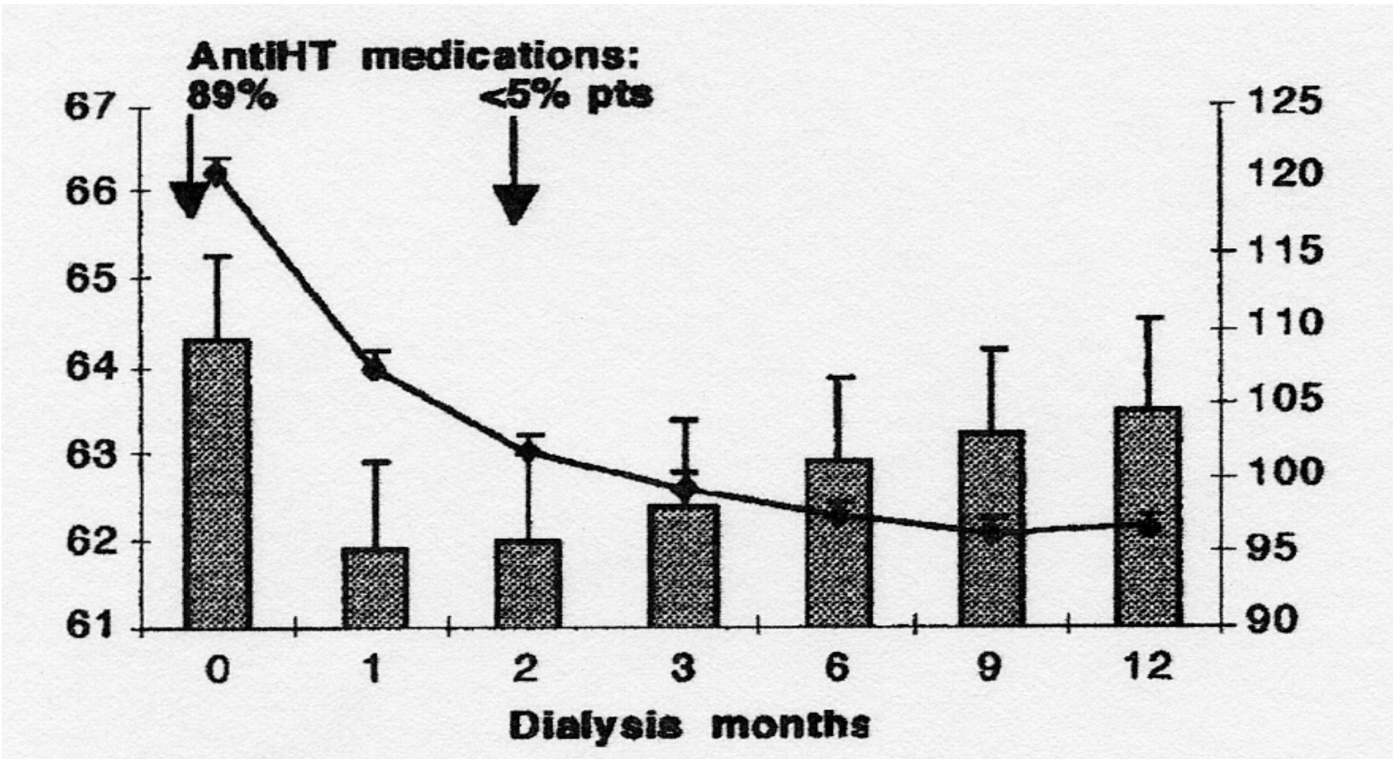
ANP







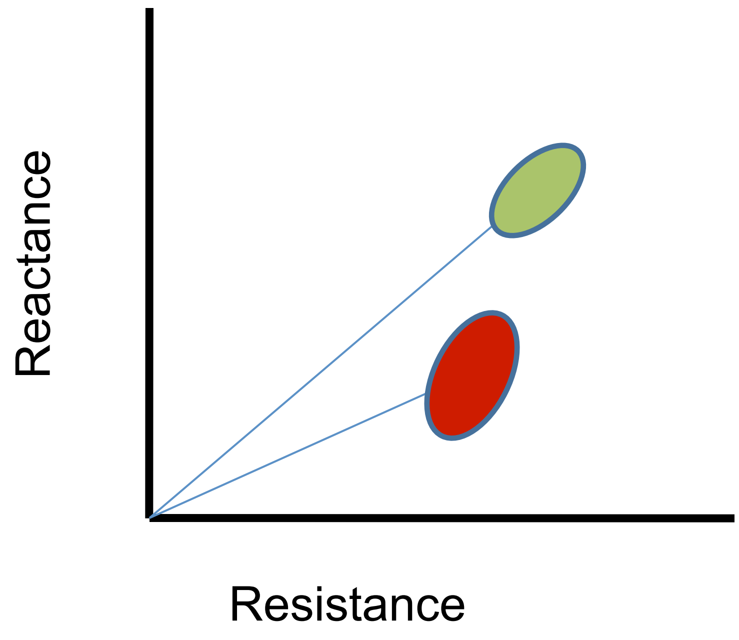
Time



712 patients in Tassin. Charra et al Am J Kidney Dis 32, 720-4, 1998

Bio-impedance techniques

Single frequency - RXc mean Plot



Piccolli et al. 1994