

Using Dialysis Prescription to Treat Hypertension in Hemodialysis Patients

Vancouver October 2010

Dr. Bob Richardson
Professor of Medicine, U of T
Director of Hemodialysis, UHN



Toronto General Hospital



Objectives

Understand:

- The difficulties of assessing BP in HD patients
- The effect of lowering dialysate sodium on BP
- The effect of lowering target weight on BP



Plan

- A Case
- Is high BP in HD patients good or bad?
- Which BP to target?
- Why is dialysate sodium concentration important?
- Can target weight be reduced in “euvolemic” patients?
- Recommendations



A Patient

- 55 year old man starts HD after failed Tx
- IgA nephritis
- Meds: Prednisone 7.5, amlodipine 5 mg, atorvastatin, calcium, rocaltrol
- RN asks what you would like to do about the patient's high BP
- TW 74 kg

Treatment Goals

- KDOQI and CSN:
 - CKD: < 130/80
 - Predialysis < 140/90
 - Postdialysis < 130/80
- Evidence level C



BP Readings Last 3 Treatments

	IDWG	Pre	Post
1	3.4	155/95	142/82
2	2.6	166/98	140/80
3	2.5	158/98	146/90
Mean	2.8	160/97	142/84



Plan

- A Case
- Is high BP in HD patients good or bad?
- Which BP to target?
- Why is dialysate sodium concentration important?
- Can target weight be reduced in “euvolemic” patients?
- Recommendations



What is the Evidence?

- Observational studies describe “reverse epidemiology”
 - Lower BP associated with poor short term outcomes
- Very few RCT’s of BP lowering in HD patients
- Meta-analysis suggests that BP lowering in HD patients reduces endpoints but indications for treatment were variable



Left Ventricular Hypertrophy in New Hemodialysis Patients without Symptomatic Cardiac Disease

Robert N. Foley,* Bryan M. Curtis,[†] Edward W. Randell,[‡] and Patrick S. Parfrey[†]

- 596 incident HD pts in Hgb trial
- Echocardiogram 1.5 to 6 years
- LVMI increased 114 to 128 g/m²
- Systolic BP predicted increase in LVMI, new LVH: OR 1.08 for every 4.1 mmHg
- Systolic BP predicted death + CV event



Hemodialysis

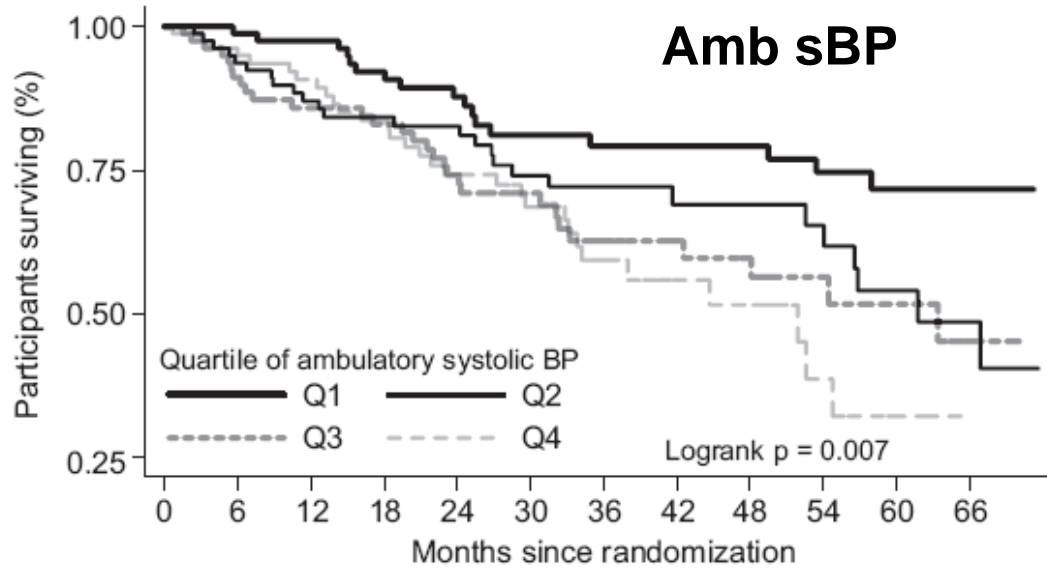
Blood Pressure and Mortality Among Hemodialysis Patients

Rajiv Agarwal

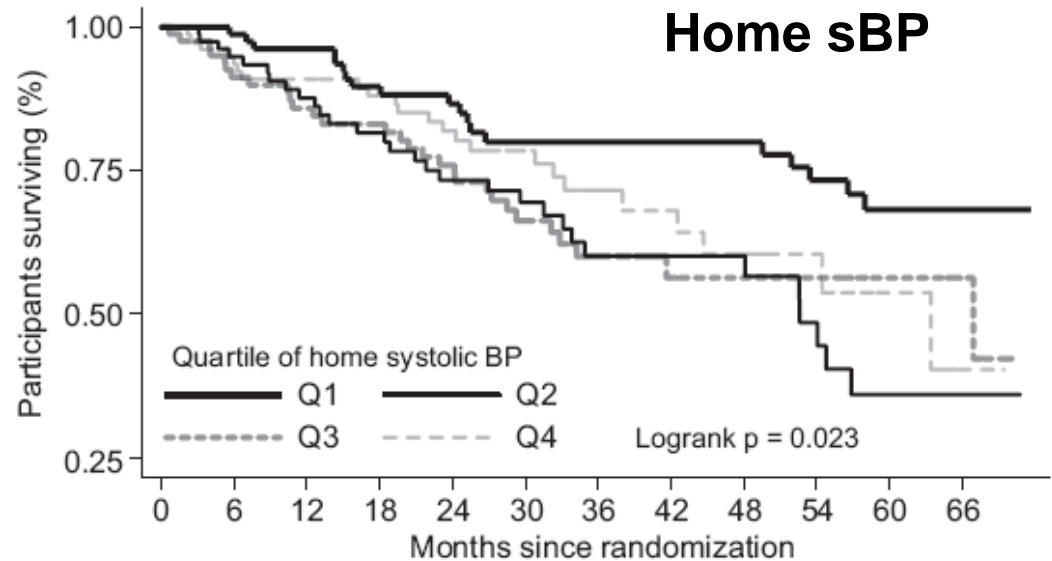
- Single center study of 326 HD pts
- Ambulatory, home and HD BPs
- 87% black
- Follow-up 3 years, 31% died
- Studied 3 methods of BP measurement related to mortality

Adjusted Hazard Ratios for Mortality by Quartiles of Amb sBP

	Mean sBP	HR	95%CI	P
Quartile 1	109±9	1		
Quartile 2	128 ±5	2.51	1.27-4.95	0.008
Quartile 3	140±4	3.43	1.73-6.79	<0.0001
Quartile 4	161 ±13	2.62	1.33-5.17	0.005



Dialysis unit
BP did not
predict all
cause
mortality





Conclusion so Far

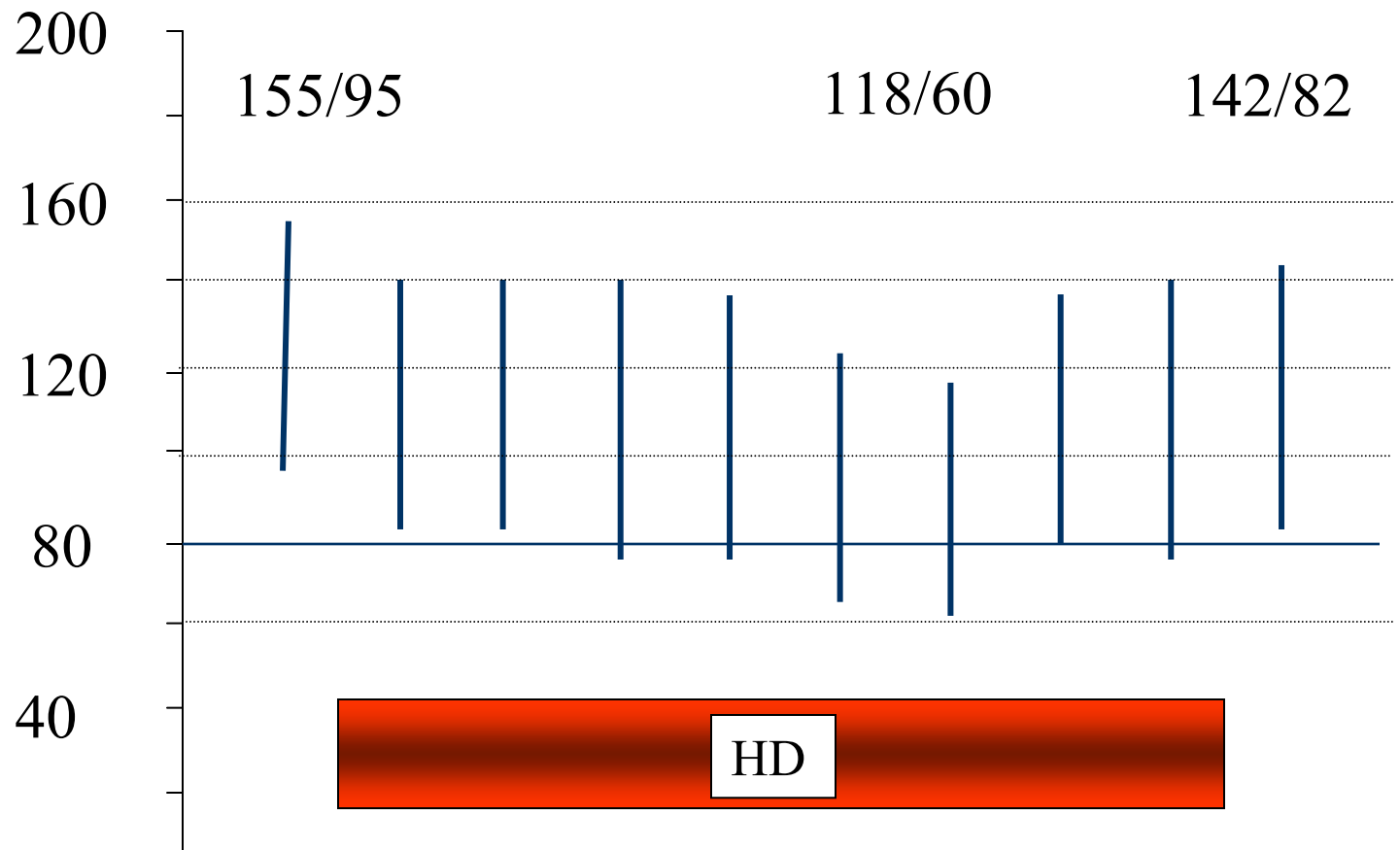
- Older data suggested high BP was associated with better outcomes
- Newer data suggests that higher BP is associated with greater risk of LVH
- Higher ambulatory or home BP, but not unit BP, is associated with increased all cause mortality



Plan

- A Case
- Is high BP in HD patients good or bad?
- Which BP to target?
- Why is dialysate sodium concentration important?
- Can target weight be reduced in “euvolemic” patients?
- Recommendations

BP variability during one HD



Sources of Variability

- Interdialytic weight gain
 - Higher predialysis than postdialysis
 - Often very low during dialysis due to fluid removal
- Stress:
 - getting to HD unit, talking, coffee, needles
- Skipping BP meds predialysis
- Non-standard BP technique

Usual vs Standardized BP in HD Patients (AJKD 2002;39:1226)

Table 2. Mean Predialysis and Postdialysis Blood Pressure Readings Obtained in the Dialysis Unit Compared With Standard Readings

		Dialysis Unit Reading (mm Hg)	Standard Reading (mm Hg)	Mean Difference in BP Between the Two Readings (mm Hg)
Predialysis	SBP	158.1 ± 26	143.8 ± 25*	14.3
	DBP	81.5 ± 17	74.5 ± 16*	7
Postdialysis	SBP	142.2 ± 28	128.6 ± 30*	13.6
	DBP	73.4 ± 16	69.0 ± 16*	4.4

* $P < 0.05$ standard reading versus dialysis unit reading.

TGH Study: Comparison of Unit BP vs BpTRU: *Hypertensives*

Unit BP	161/81
BpTRU	134/76
Δ BP	27/13
% with “White coat” hypertension	54%

M M Sood, M Battistella, C E Lok, R Richardson

What are the Choices?

- ABPM - ideal, not very practical
- Home BP
- BP on non-dialysis day - great for self care, home HD patients seen in clinic
- Predialysis/Postdialysis BP
- Mid-week median BP during dialysis:
 - Cutoff systolic of 140 provides 80% sensitivity and 80% specificity for hypertension defined by 44 h ABPM of > 135/85 (Agarwal JASN 2008)

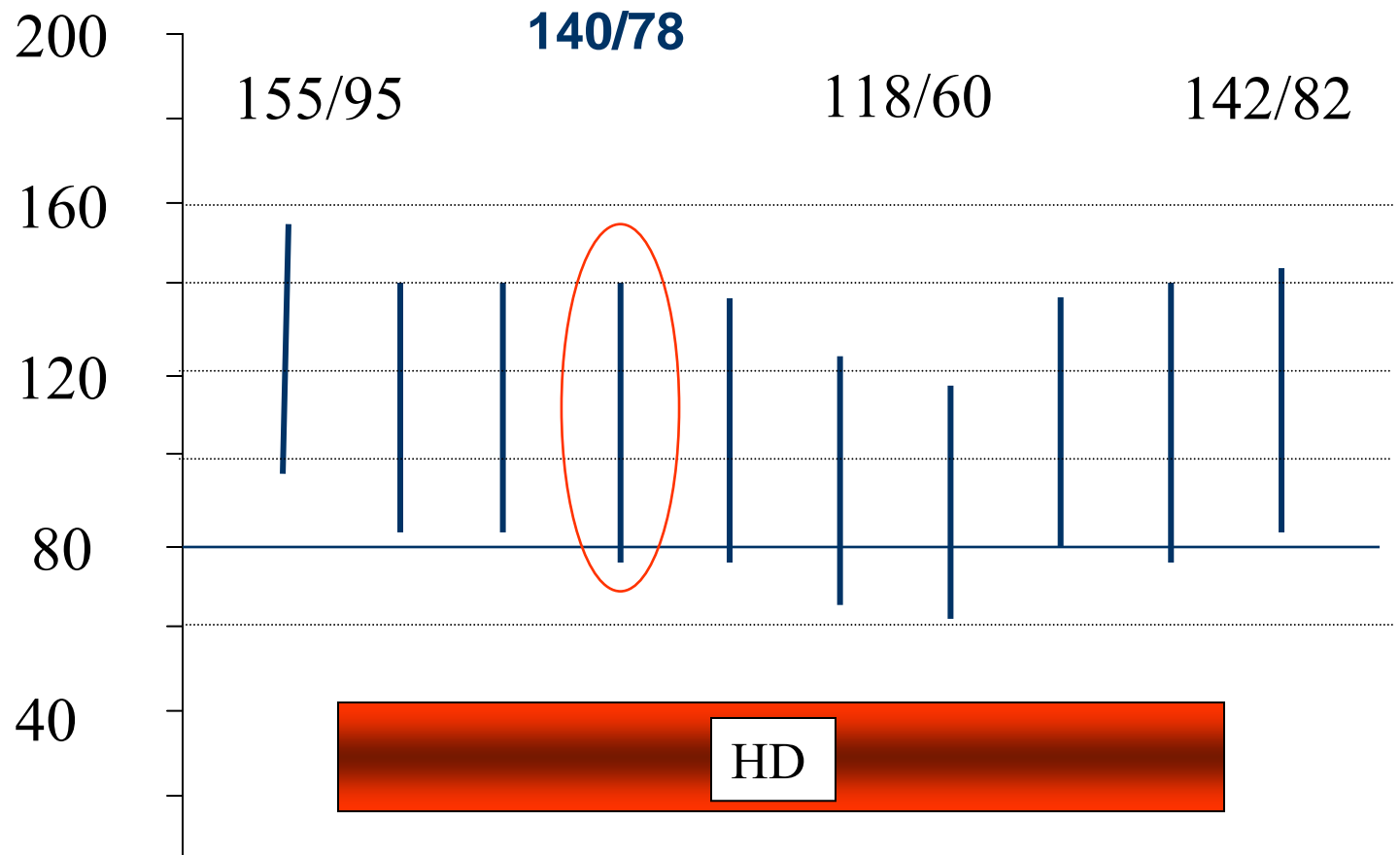


Median Intradialytic Blood Pressure Can Track Changes Evoked by Probing Dry-Weight

Rajiv Agarwal*[†] and Robert P. Light*

- In DRIP study, median intradialytic BP corresponded with change in ambulatory sBP better than either pre- or post-dialysis sBP
- However SD of difference was large
- Ambulatory BP is best, but median intradialytic BP is next best

BP variability during one HD



Measurement: Conclusion

- Casual predialysis BP measurements are of no value
- Midweek median BP may be excellent surrogate for ABPM



Plan

- A Case
- Is high BP in HD patients good or bad?
- Which BP to target?
- Why is dialysate sodium concentration important?
- Can target weight be reduced in “euvolemic” patients?
- Recommendations



Dialysate Sodium and BP: Postulate

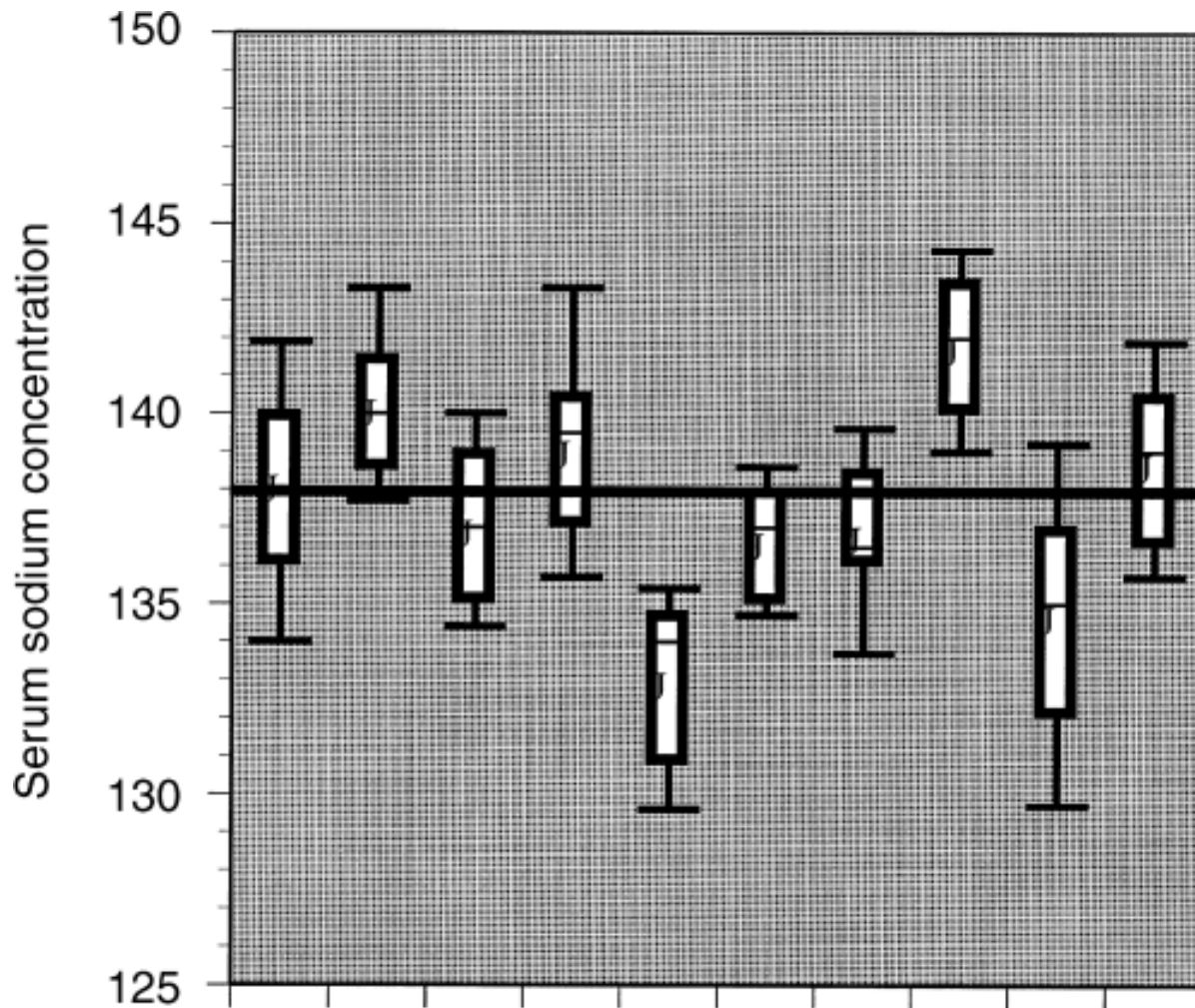
- Predialysis PNa^+ is constant in individuals but varies between individuals on HD
- Mean predialysis PNa^+ in HD pts $\ll 140$ mM
- If $dNa^+ > PNa^+$:
 - Increased thirst and weight gain
 - Increased ECFV and sodium content
 - Hypertension

Importance of ECF Volume and Total Body Sodium

- Interdialytic weight gain is mainly in the extracellular fluid
- Ranges from 0 to 7% of Body Weight
 - Up to 35% increase in ECFV and Na⁺
- Major contributor to:
 - Hypertension
 - Mortality

Conclusion: minimize interdialytic wt gain

Predialysis Serum Sodium in HD Patients



In individual HD patients there is little variation in pre-HD serum sodium over 12 months.
Mean = 136-138

Flanagan
KI 2000

Blood Purification
2010:29:264

Effect of Reducing Dialysate [Na]?

- At same target weight but lower serum sodium concentration:
 - Higher intracellular volume
 - Lower extracellular volume
 - Lower ECF sodium content
- Less interdialytic weight gain because of less thirst; less intradialytic hypotension
- Theoretically should reduce blood pressure and interdialytic BP increase

Association of ΔNa with Adverse Outcomes in HD Patients

In 2187 HD patients, dialysate $\text{Na} \geq 140$ mmol/L was associated with:

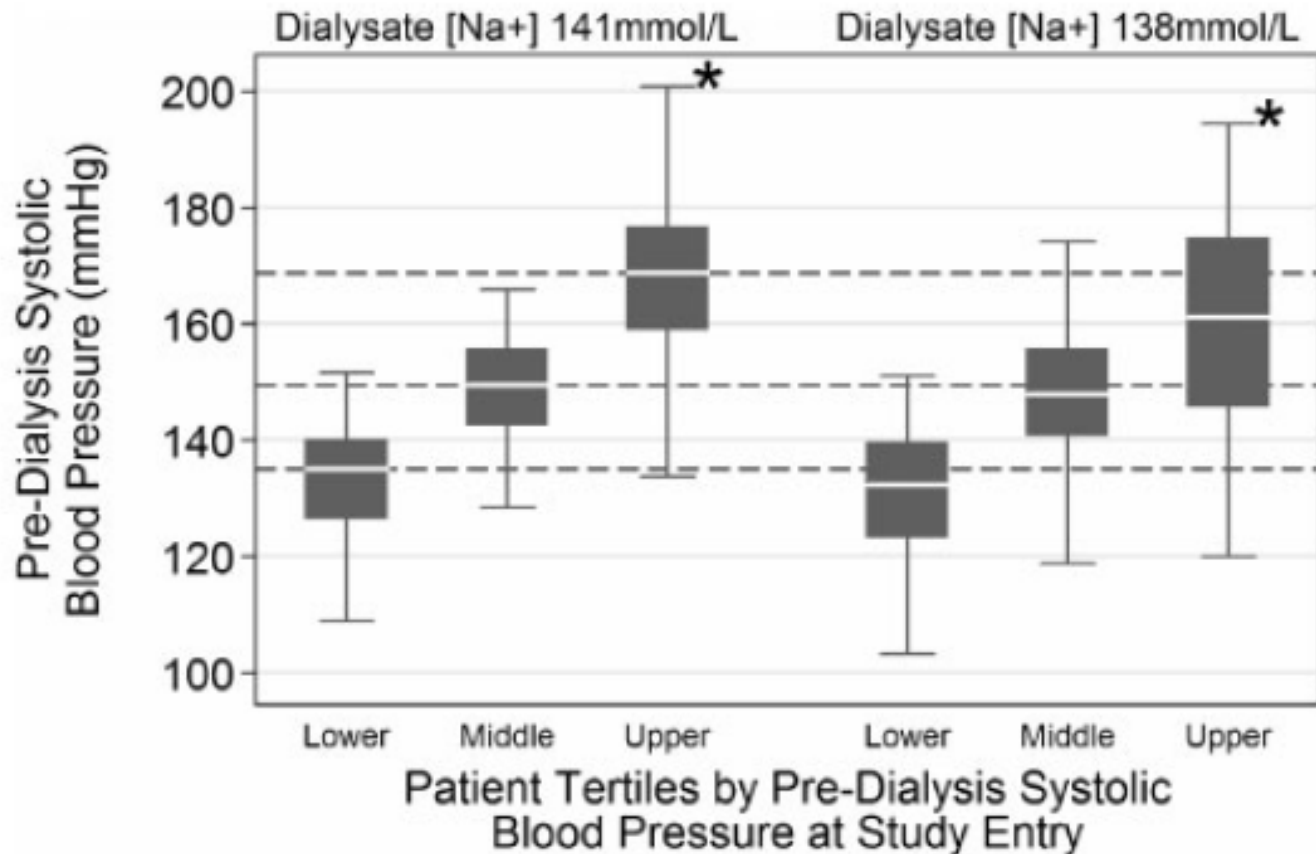
- More IDWG
- Higher pulse pressure
- More intradialytic hypotension requiring saline

Effect of Individualized Dialysate Sodium on HD Patients with High BP

	Standard sodium	Individualized sodium
Pre-HD plasma sodium	134.0 ± 1.4	134.0 ± 1.5
Post-HD plasma sodium	135.9 ± 2.0	133.1 ± 2.6
IDWG (kg)	2.91 ± 0.87	2.29 ± 0.87
Interdialytic thirst, <i>n</i> (%)		
Nil	0 (0)	4 (15)
Mild	1 (4)	17 (63)
Moderate	11 (41)	5 (18)
Severe	15 (55)	1 (4)
Hypotensive episodes, <i>n</i> (%) of sessions	23 (9)	6 (2)

In hypertensive patients, Δ BP = -16/7

Effect of Unit-wide Reduction of Dialysate Sodium



In highest tertile, sBP fell from 169 to 161.
 Δ IDWG fell from 3.2 to 2.9 kg (NS)



Dialysis

Lowering Postdialysis Plasma Sodium (Conductivity) to Increase Sodium Removal in Volume-Expanded Hemodialysis Patients: A Pilot Study Using a Biofeedback Software System

Jaimi Manlucu, MD, FRCPC, Kerri Gallo, RN, CNS, Paul A. Heidenheim, MSoc, and Robert M. Lindsay, MD, FRCPC, FRCP(Edin), FRCP(Glasg)

- 16 HD pts over 7 wks
- Post-dialysis PNa^+ lowered from 138 to 135 in 4 stages
- No change in TW
- Used BIA to measure ECFV

Effect of Lowering Post-dialysis PNa⁺

	Phase 1	Phase 4	P
Post PNa ⁺	138.5	135.6	
Ionic mass balance	382	480	<0.001
%ECW	51.8	49.3	0.001
sBP	147	136	0.02
IDWG	2.8	2.1	0.04

Comparison of High Sodium and Neutral Sodium Profiles

J Am Soc Nephrol 16: 237–246, 2005.

	PS + U	NS + U
Intradialytic symptoms	24%	24%
UF failure	18%	18%
Interdialytic symptoms	36%	15%
% wt gain > 7%	27%	9%
% ↑ BP > 10%	15%	6%

Conclusion

In HD patients with hypertension or excessive interdialytic weight gain:

- Set dialysate sodium equal to or lower than average predialysis sodium
 - Reduces IDWG, thirst, BP, and intradialytic hypotension
- If sodium profiling is required, set mean dialysate sodium to equal average predialysis sodium



Plan

- A Case
- Is high BP in HD patients good or bad?
- Which BP to target?
- Why is dialysate sodium concentration important?
- Can target weight be reduced in “euvolemic” patients?
- Recommendations



Target Weight Reduction

- Well known association between sodium content, ECFV and BP
 - Diuretics for hypertension
 - Restricted sodium diet for hypertension
 - Increase in BP with interdialytic wt gain
- Does lowering target weight for the indication of hypertension alone work?

Dry-Weight Reduction in Hypertensive Hemodialysis Patients (DRIP)

A Randomized, Controlled Trial

Rajiv Agarwal, Pooneh Alborzi, Sangeetha Satyan, Robert P. Light

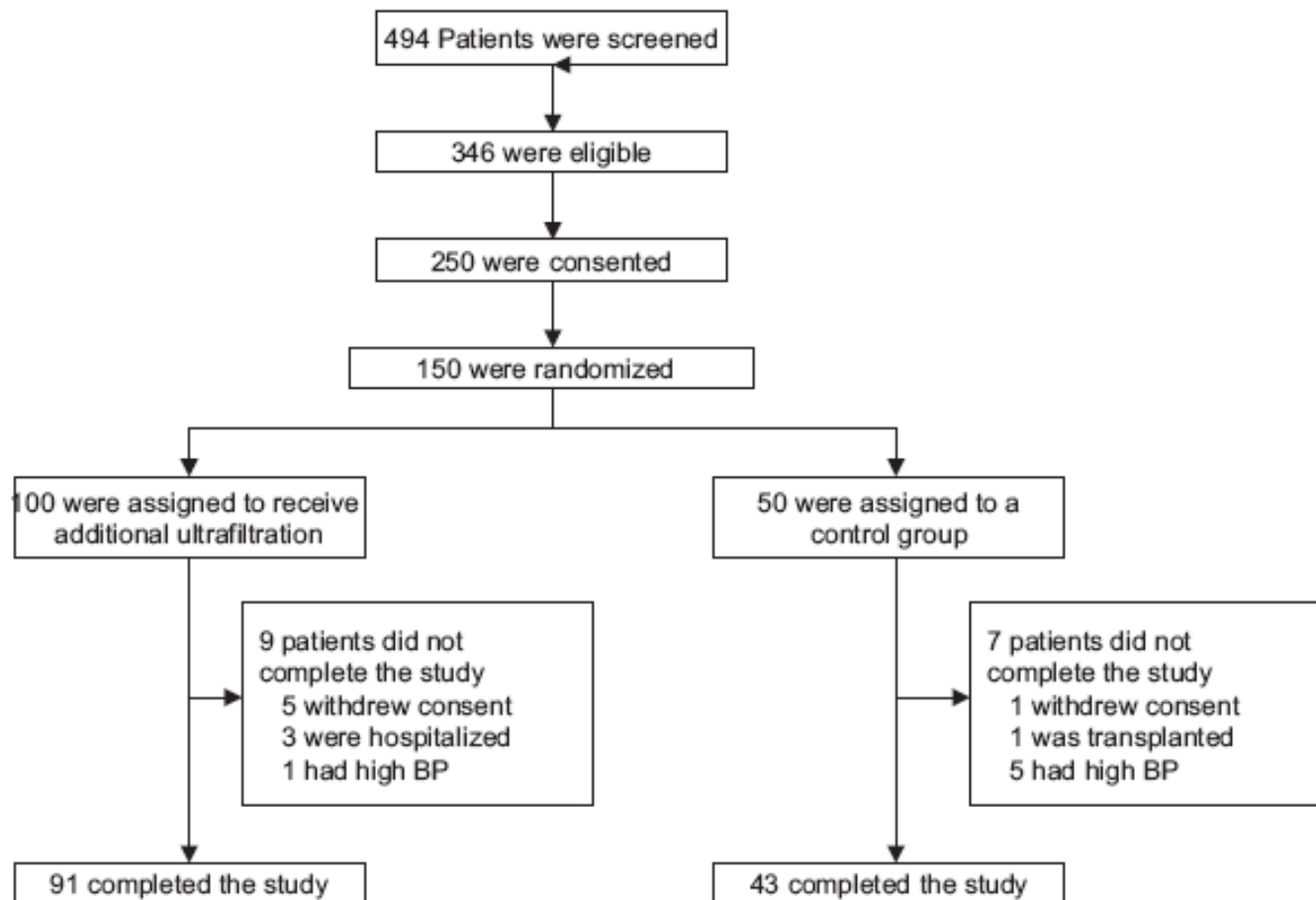
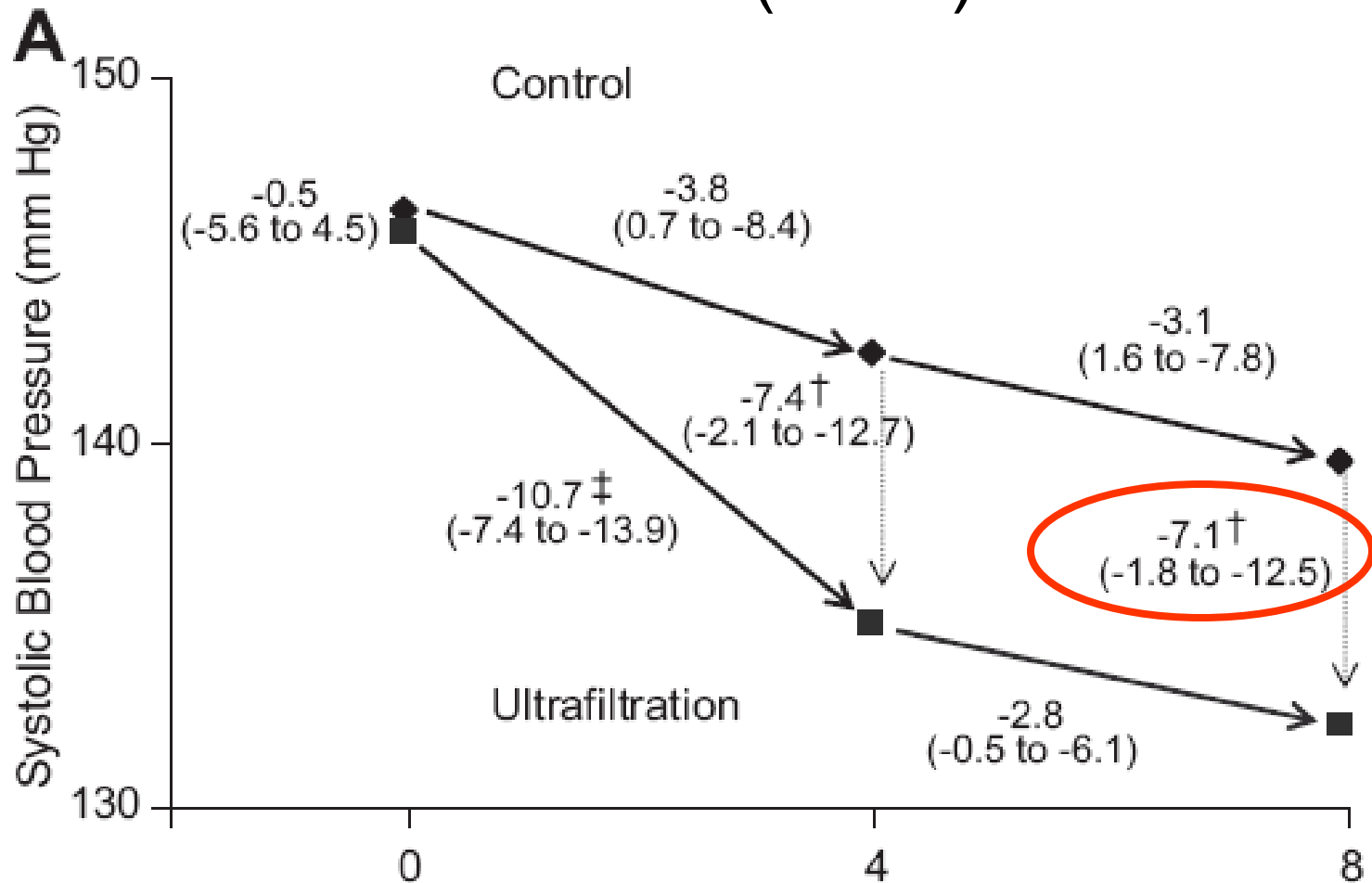


Figure 1. Enrollment and trial flow.

(Hypertension. 2009;53:500-507.)

Change in ABPM Attributable to Reduction in TW (1.0 L)





Conclusion

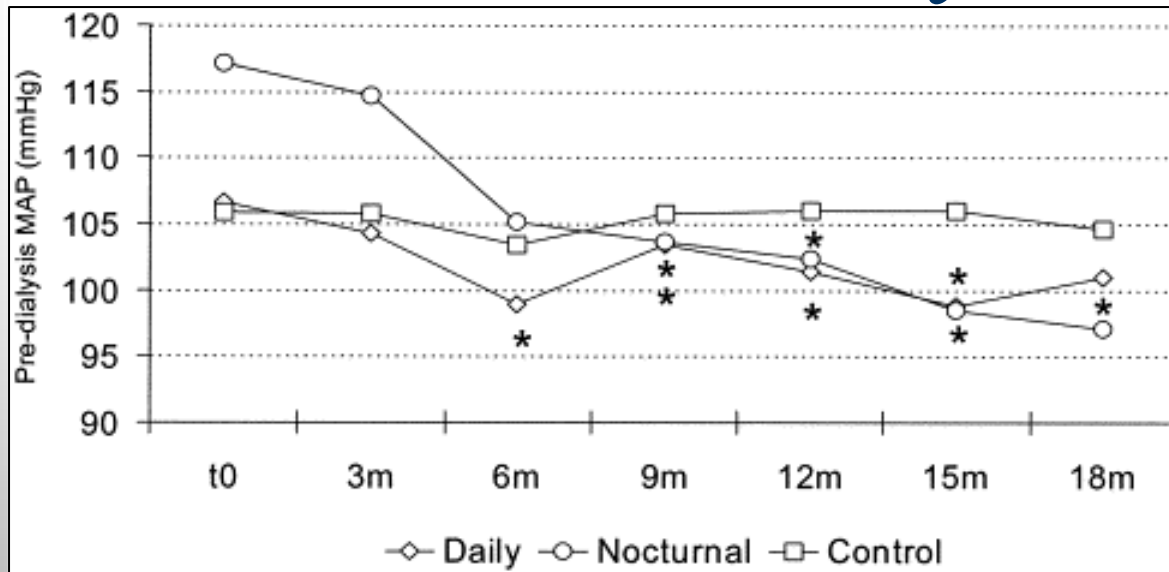
- Many studies and clinical experience indicate that target weight can be reduced in hypertensive dialysis patients with no signs or symptoms of volume overload
- Should be done slowly
- BP effect may be delayed by weeks



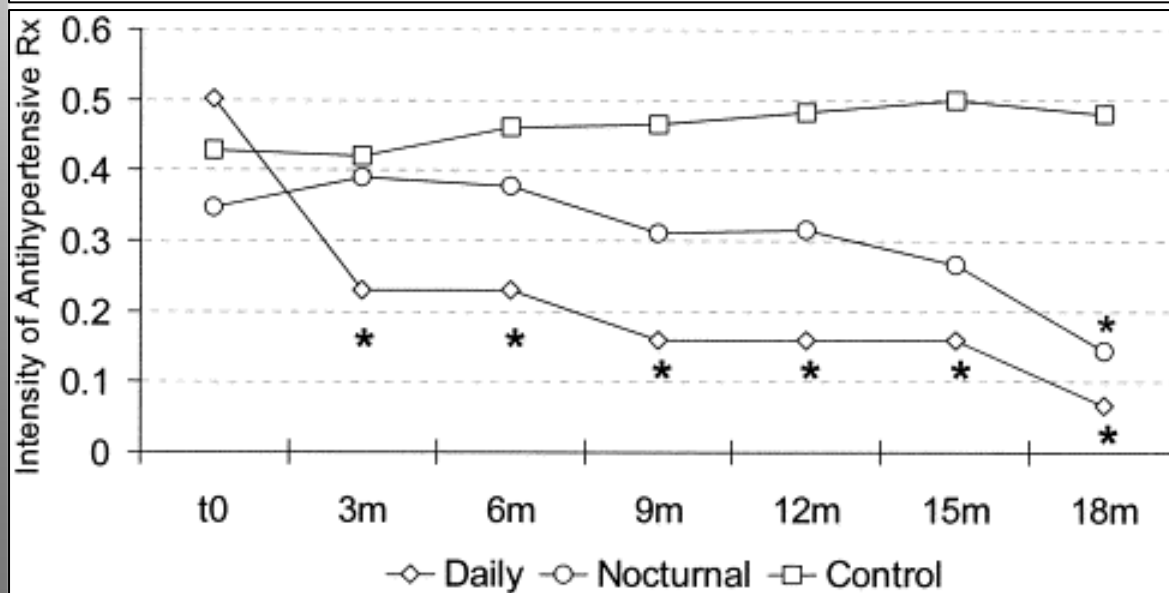
Other Dialytic Methods to Lower BP

- Increase frequency of dialysis
 - Short daily HD
 - 2-2.5 h X 5-6 treatments/week
- Increase frequency and duration of dialysis
 - Nocturnal home hemodialysis
 - 6- 8 h X 4-6 treatments/week

London Short Daily HD Study



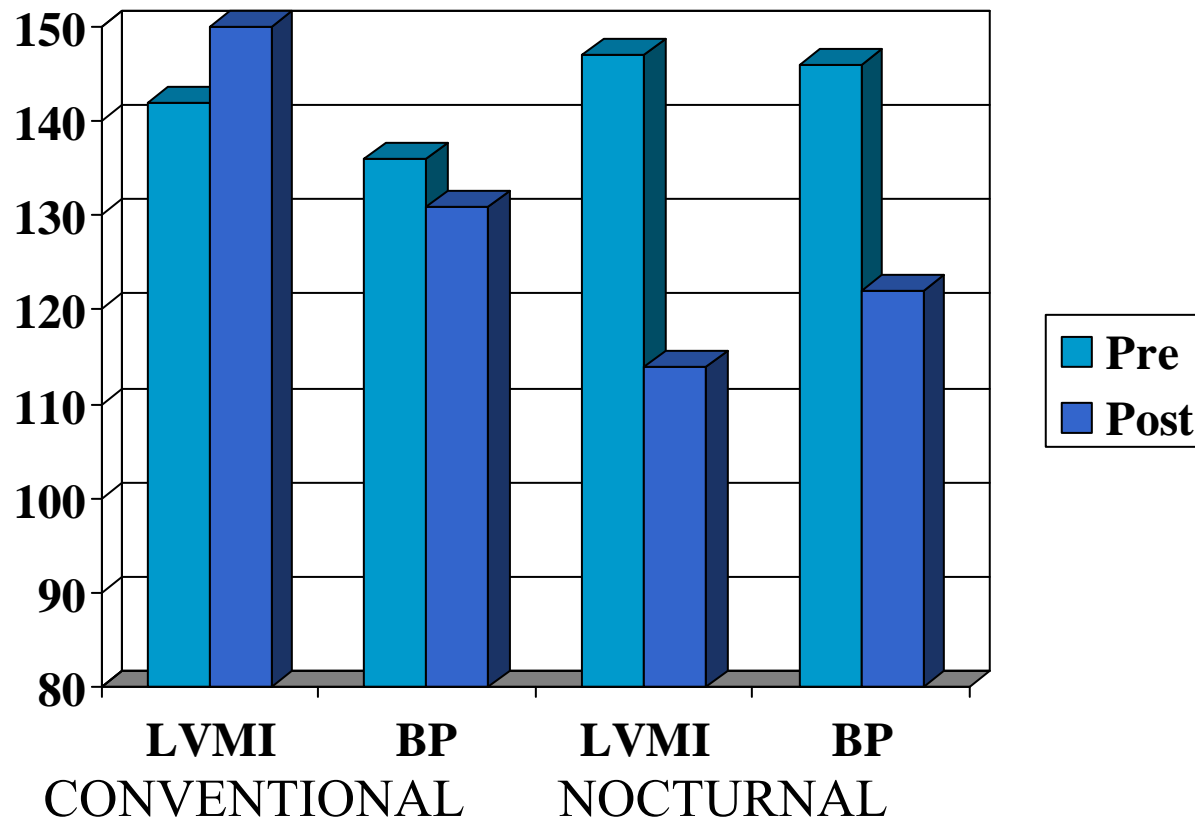
MAP



BP meds

AJKD 2003

Effect of Nocturnal HD on LVMI and BP



Chan, Kidney Int 2002



Conclusions

- Longer and/or more frequent HD lowers BP
- Lowering dialysate Na^+ lowers BP
- Slow reduction in TW in “euvolemic” patients lowers BP
- The latter two techniques have no associated cost or compliance issues



What We Don't Know

- What should the target BP be?
- Should target BP be related to age, dialysis vintage, comorbidity?
- Is non-pharmacologic BP reduction as useful as pharmacologic?



My Recommendations

- Use median intradialytic BP over several treatments to determine BP
- Use target weight reduction and dialysate sodium reduction aggressively to reduce IDWG and BP
- Minority of patients will need antihypertensives to get median BP < 135/85