Recent Advances In the Prevention Of Hypotension During Hemodialysis

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Agenda

- **Definition of Intradialytic Hypotension (IDH)**
- **Pathophysiology of IDH**
- **Strategies and Maneuvers to Prevent IDH**
  - Pharmacological
  - Na and UF profiling
  - BVM and Automatic Biofeedback
  - BTM and Cooling
  - HDF
- **Review of major clinical studies**
- **Conclusion**

Intra-dialytic hypotension (IDH)

- Definition:

  Decrease in systolic BP by ≥20 mmHg or decrease in MAP by 10 mmHg

  in combination with hypotensive symptoms

  and need for nursing intervention

  nadir-based IDH, cut-off SBPs of 90 and 100 mmHg

K/DOQI clinical practice guidelines. *Am J Kidney Dis* 45:Suppl 3:S1, 2005
Kooman J et al., EBPG guideline. *Nephrol Dial Transplant* 22:Suppl 2:ii22, 2007
Flythe JE et al, Association of motality risk with IDH. *J Am Soc Nephrol* 26:724-734, 2015

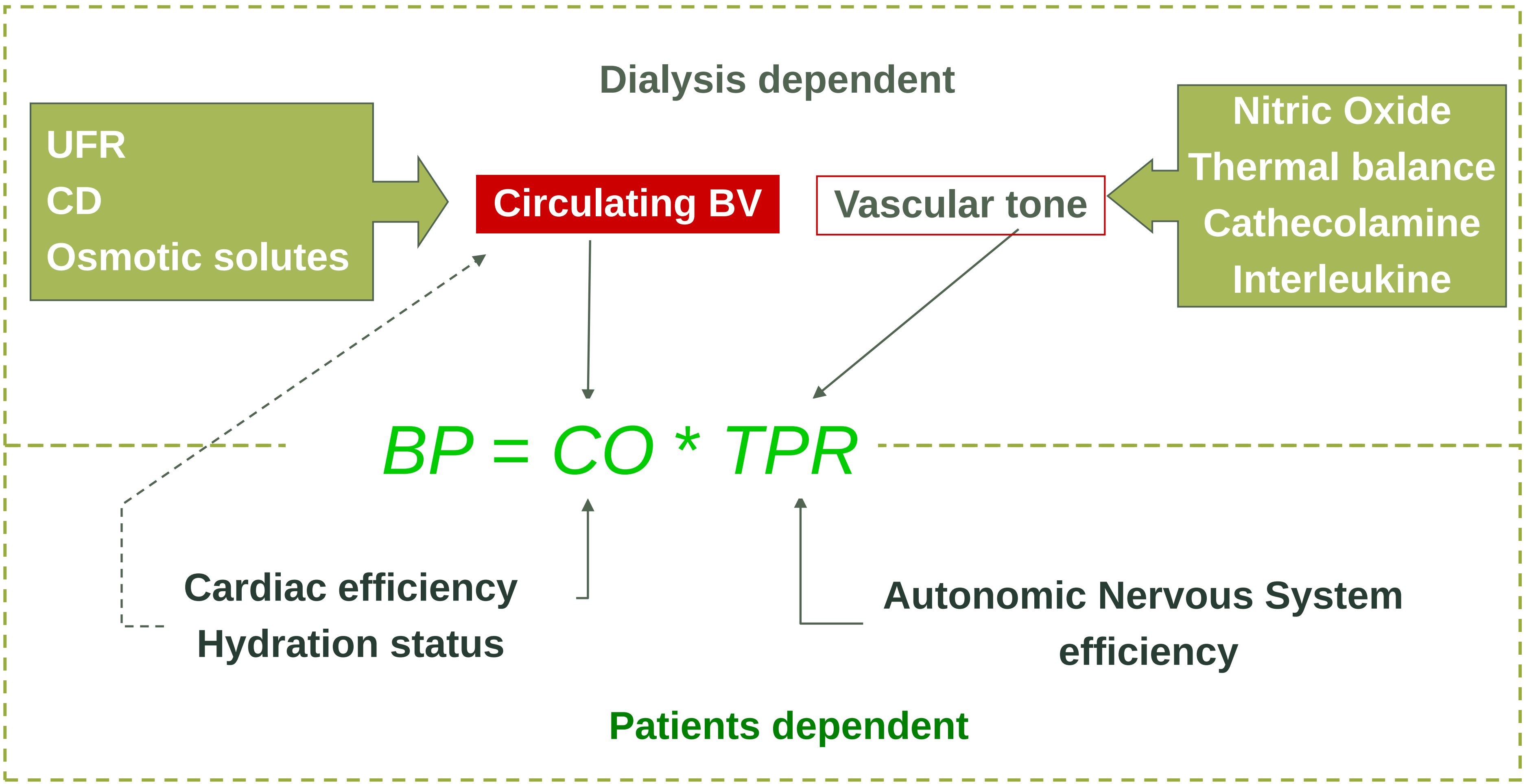
- One of the most frequent complications of hemodialysis

  : 20~30% of all hemodialysis sessions

Concerns about IDH

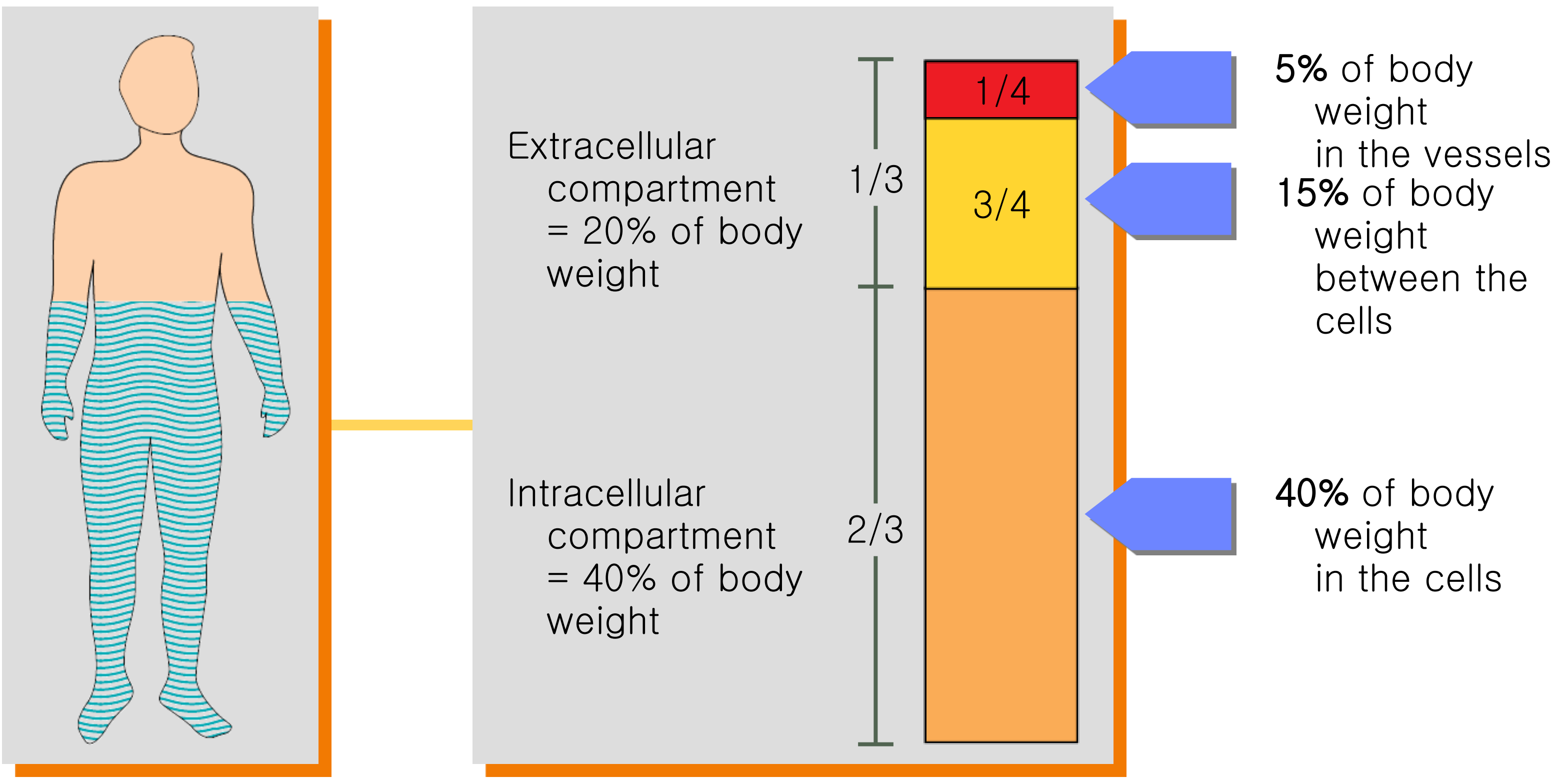
- Symptomatic discomfort
- Chronic fluid overload : HTN and LVH
- Reduced solute clearance
- Myocardial ischemia, Repeated
  - Perfused during diastole
  - Increased mortality

Determinants of Arterial Pressure during hemodialysis

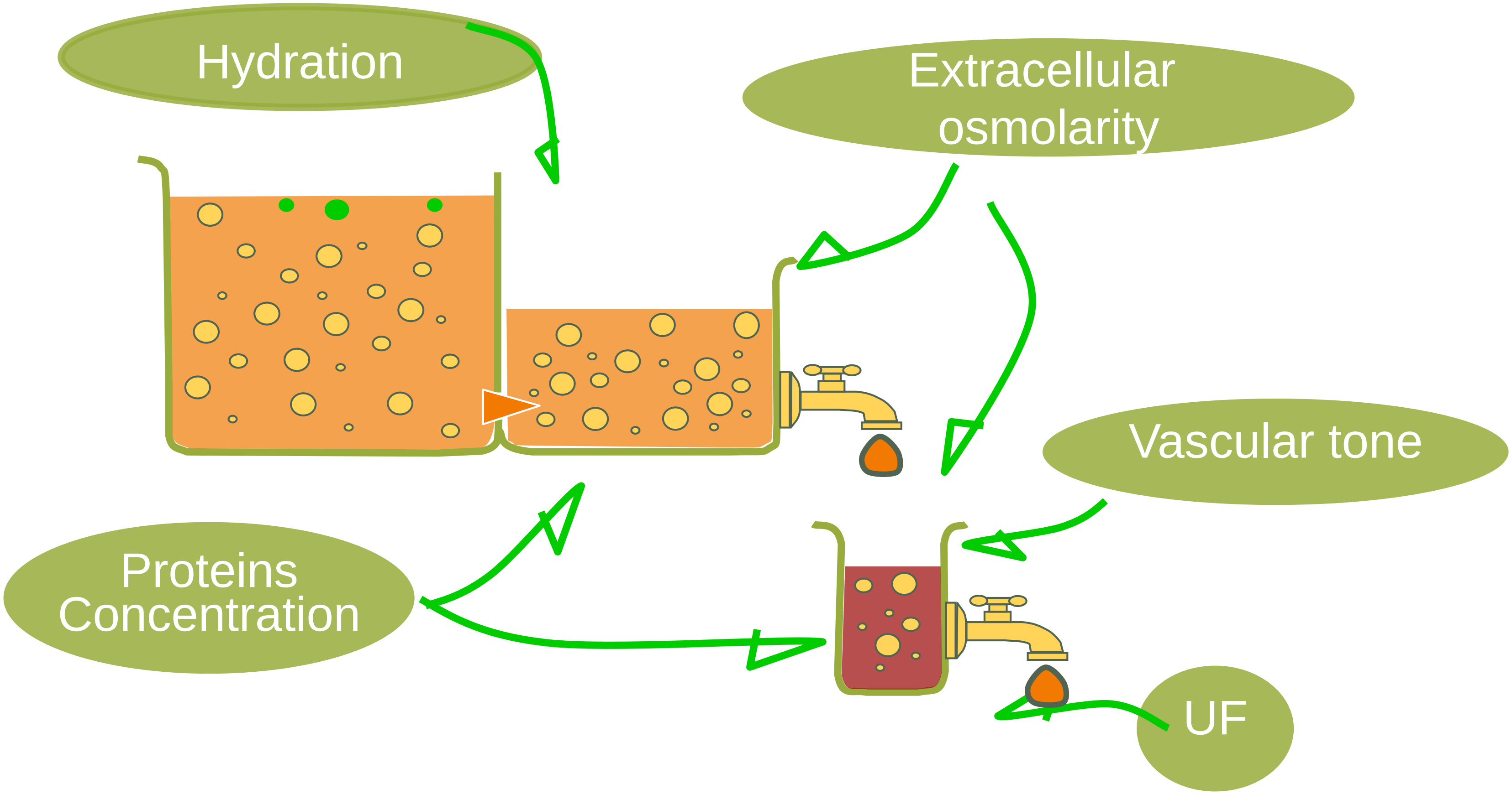


Fluid removal during dialysis

- Volume distribution



Factors affecting plasma refilling rate during dialysis

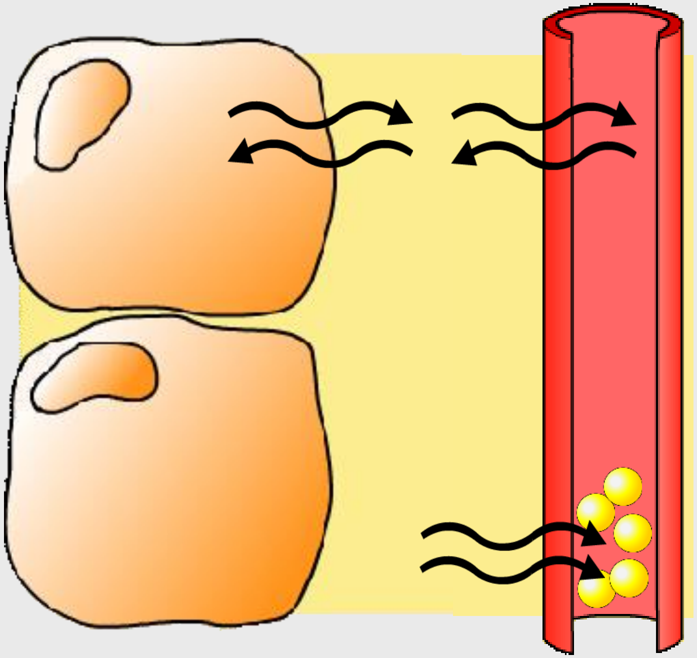


Principles of fluid removal

Blood volume change and refilling

Factors affecting refilling:

- Overhydration
- Plasma osmolarity
- Protein concentration
- UF rate
- Patient`s refill capability



EBPG guideline on hemodynamic instability

5. Stratified approach to prevent IDH

First-line approach

- Dietary counseling (sodium restriction).
- Refraining form food intake during dialysis.
- Clinical reassessment of dry weight.
- Use of bicarbonate as dialysis buffer.
- Use of a dialysis temperature of 36.5°C.
- Check dosing and timing of antihypertensive agents.

Second-line approach

- Try objective methods to assess dry weight.
- Perform cardiac evaluation.
- Gradual reduction of dialysate temperature from 36.5° downward (lowest 35°C) or isothermic treatment (possible alternative: convective treatments).
- Consider individualized blood volume controlled feedback.
- Prolong dialysis time and/or increase dialysis frequency.

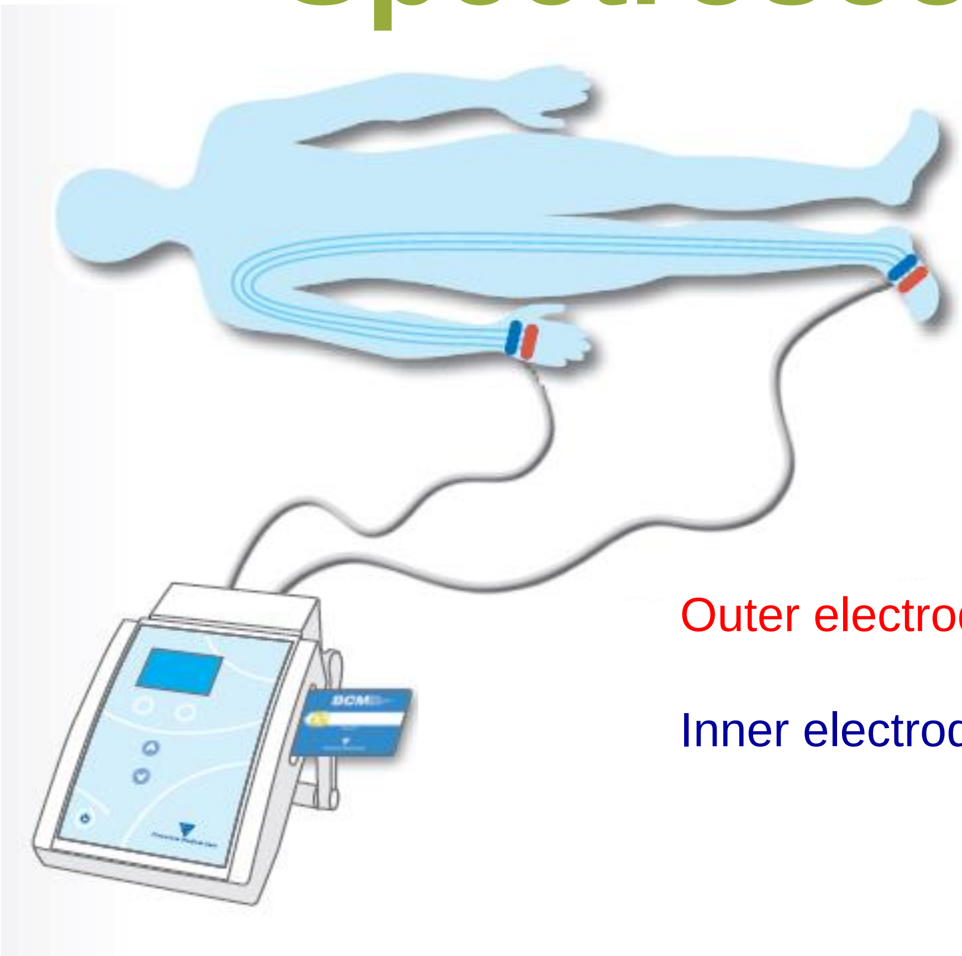
Pharmacological Maneuvers for IDH

- Midodrine
  - 10mg, single oral dose 5-30min before HD
  - Safe and effective, but variable results
- Arginine vasopressin
  - A relative AVP deficiency during HD
  - Continuous IV infusion or Intranasal DDAVP
- Adenosine A1 receptor antagonists

Technical Maneuvers for IDH

- Objective assessment of dry weight : BCM® , S10®
- Handling dialysis treatment time, dialysis frequency & Ultrafiltration rate
- Sodium profiling & UF profiling
- Cold dialysate
- Blood volume monitoring
- Using biofeedback technology : Hemocontrol® / BTM ® to control blood volume reduction during dialysis

Bioimpedance Spectroscopy (BIS)



Outer electrodes (red): Apply electrical current

Inner electrodes (blue): Measure voltage

$$\text{Impedance} = \frac{\text{voltage}}{\text{current}}$$

Effect of BIS-guided volume assessment on IDH

- IDH was more common among patients with hypovolemia assessed by M-BIA. M-BIA readily identified patients where IDH could be prevented by increasing dry weight. Kalainy S et al. *Can J Kidney Health Dis* 2015; 2
- The frequency of IDH was not decreased despite the use of M-BIA in conjunction with adjustment of UFR.
  Hur E et al. *Am J Kidney Dis* 2013; 61

Dialysis treatment time, dialysis frequency and UFR

- Limit Interdialytic weight gain (IDWG) : ≥ 3kg or ≥ 3% of estimated dry weight occurs more frequently among patients with IDH.
  - Counsel patient regarding salt intake and habitual drinking
  - Prevent hyperglycemia in diabetes
  - Utilize diuretics at high doses in patients with residual renal function

- Some experts recommend that when prescribing dialysis time, it is important to consider that the maximum UFR should not exceed 10 mL/kg/h

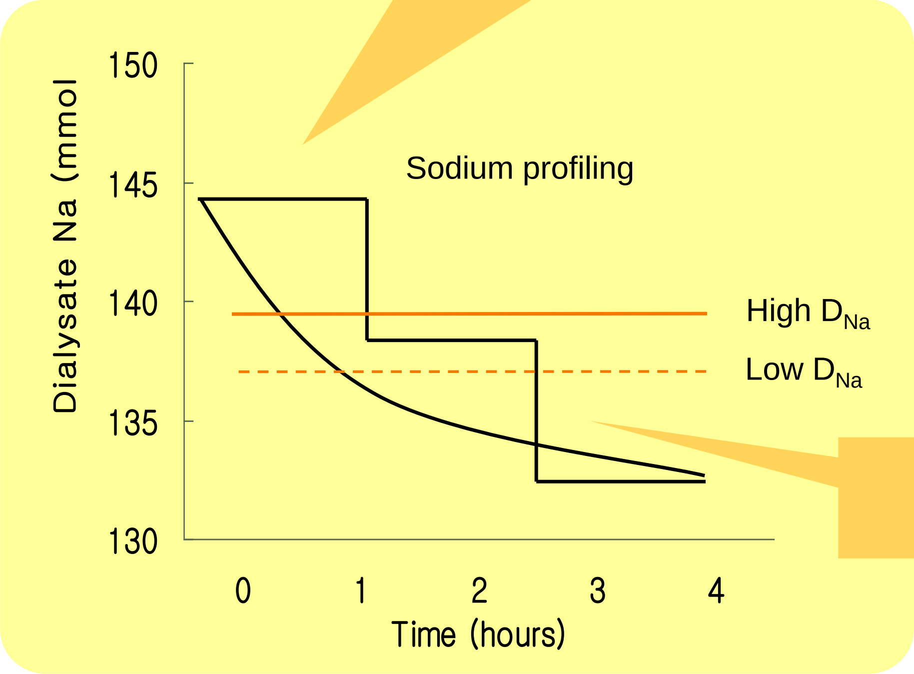
- More frequent or longer treatments that allow for lower UFR likely lessens the risk of IDH, but may result in more frequent episodes of IDH, if total ultrafiltration exceeds the target, if the target weight is underestimated.

Sodium Profiling Hemodialysis

- Time-dependent profile of high ~ low D_{Na}

  : period to maintain plasma tonicity ~ to compensate Na load

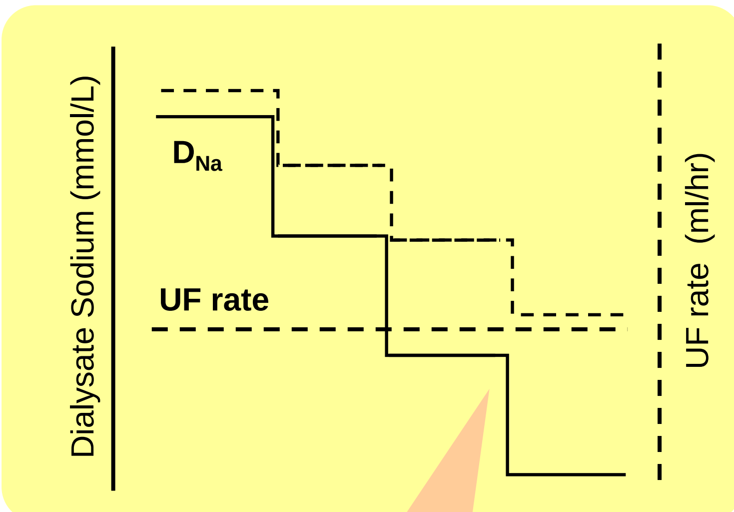
High D_{Na} to increase plasma Na & tonicity
↑ Plasma refilling = ↓ IDH



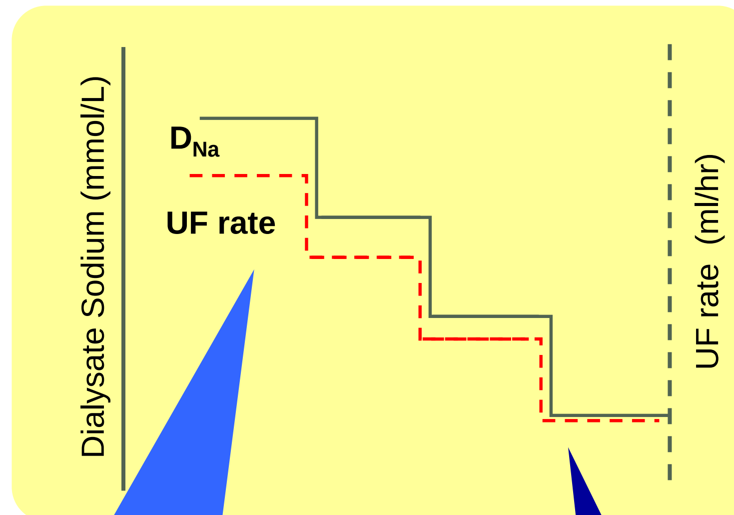
Low D_{Na} to compensate
sodium gain

SPHD + UF Profiles is Essential

SPHD with constant UF



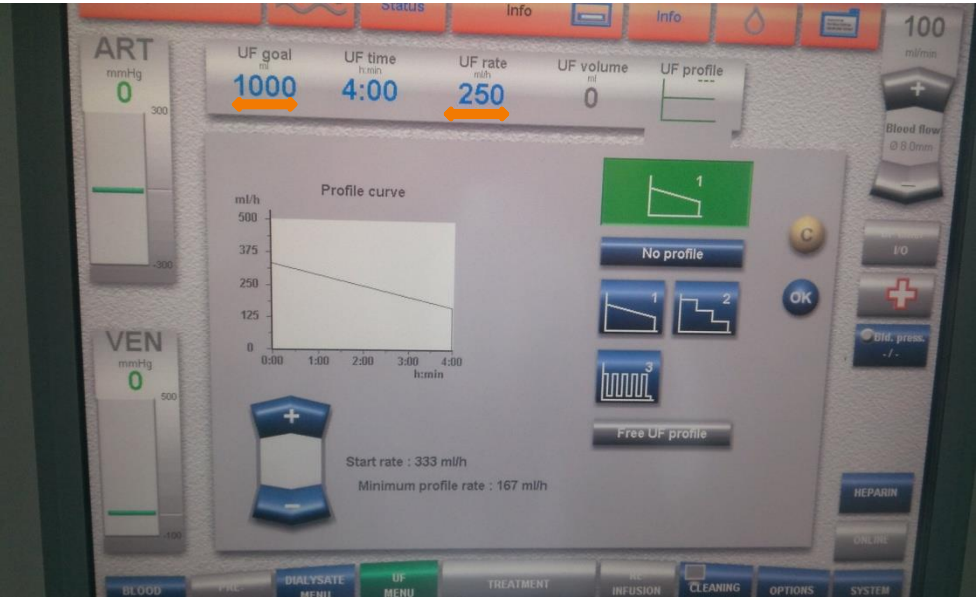
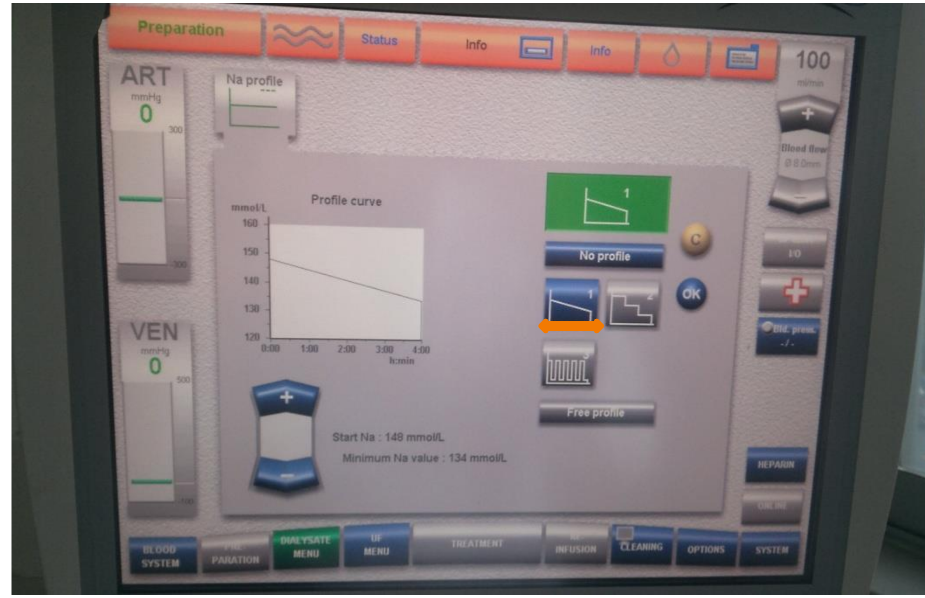
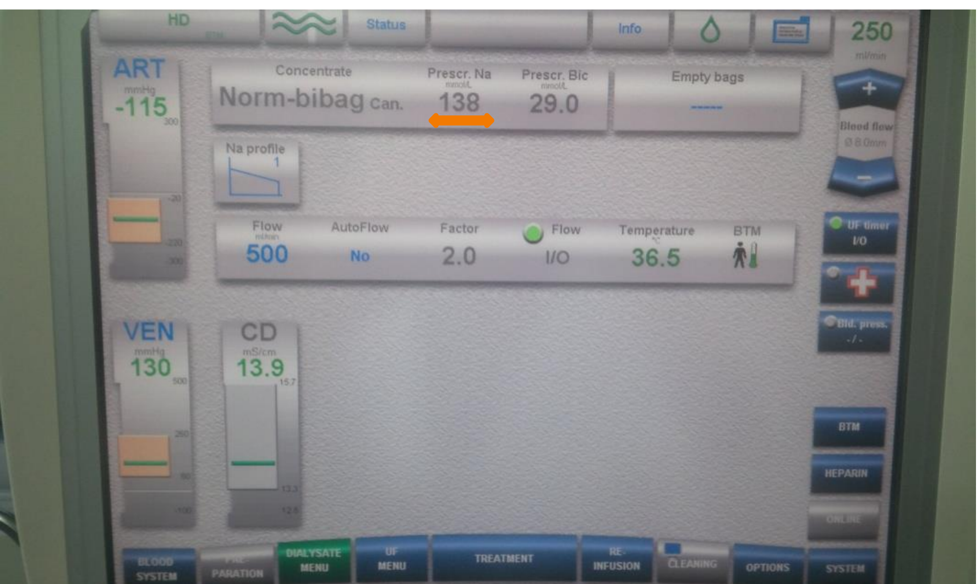
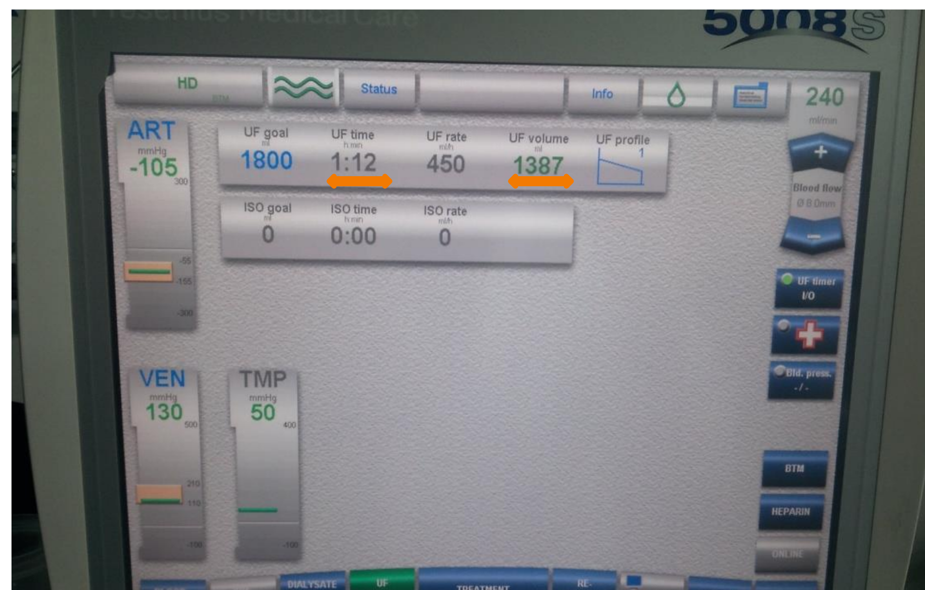
SPHD with UF profiles



Constant UF rate
- low plasma volume
- low P_{Na}/oncotic pressure
- high risk for IDH

High UF rate
- high plasma volume
- high P_{Na}/oncotic pressure

Low UF rate
- low plasma volume
- low P_{Na}/oncotic pressure
- ↓ high for IDH


Status
Info
Info
100
ART
mmHg
0
UF goal
1000
UF time
4:00
UF rate
250
UF volume
0
UF profile
Profile curve
ml/h
500
375
250
125
0
0:00
1:00
2:00
3:00
4:00
h:min
No profile
Free UF profile
OK
VEN
mmHg
0
Start rate : 333 ml/h
Minimum profile rate : 167 ml/h
HEPARIN
Blood flow
I/O
Bld. press.
TREATMENT
INFUSION
CLEANING
OPTIONS
SYSTEM

Preparation
Status
Info
Info
100
ART
mmHg
0
Na profile
Profile curve
mmol/L
160
150
140
130
120
0:00
1:00
2:00
3:00
4:00
h:min
No profile
Free profile
OK
VEN
0
Start Na : 148 mmol/L
Minimum Na value : 134 mmol/L
HEPARIN
BLOOD SYSTEM
DIALYSATE MENU
TREATMENT
INFUSION
CLEANING
OPTIONS
SYSTEM

HD
Status
Info
250
ART
-115
Concentrate
Norm-bibag can.
Prescr. Na
138
Prescr. Bic
29.0
Empty bags
Na profile
Flow
500
AutoFlow
No
Factor
2.0
Flow
I/O
Temperature
36.5
BTM
VEN
130
CD
mS/cm
13.9
UF timer
I/O
Bld. press.
BTM
HEPARIN
BLOOD SYSTEM
PRE-PARATION
DIALYSATE MENU
UF MENU
TREATMENT
RE-INFUSION
CLEANING
OPTIONS
SYSTEM

5008S
HD
Status
Info
240
ART
-105
UF goal
1800
UF time
1:12
UF rate
450
UF volume
1387
UF profile
ISO goal
0
ISO time
0:00
ISO rate
0
VEN
130
TMP
mmHg
50
UF timer
I/O
Bld. press.
BTM
HEPARIN
DIALYSATE MENU
UF MENU
TREATMENT
RE-INFUSION
CLEANING
OPTIONS

Problem of SPHD: Sodium Load

- Dialysate sodium up to 138~140 mEg/L

Diffusive
Sodium Gain

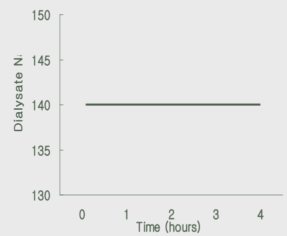
Intradialytic period

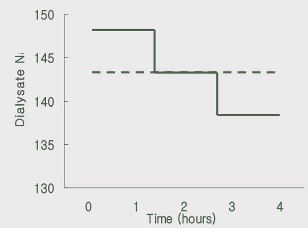
↓IDH & its related morbidities

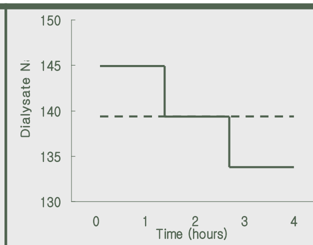
Interdialytic period

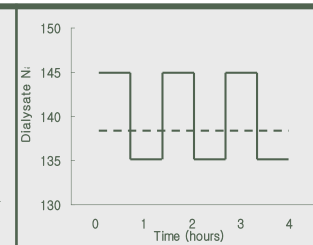
↑Cx d/t sodium gain
(thirst, weight gain,
Hypertension)

Just shifting the time of dialysis
discomforts ?









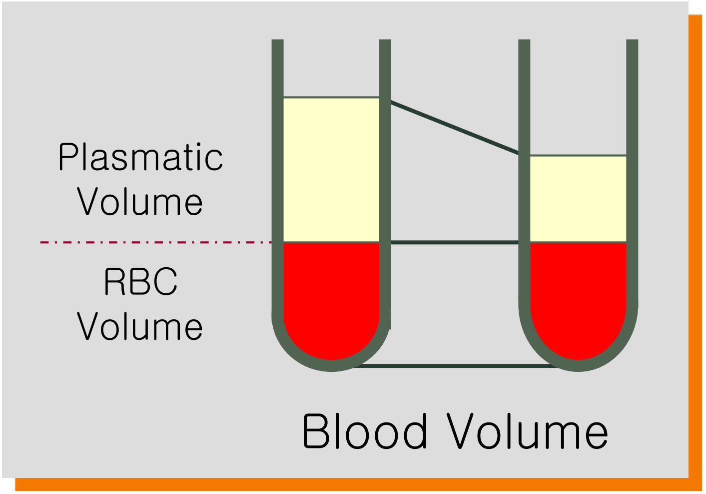
Na balance			**P**ositive	**N**eutral	**N**eutral
		Convention	**S**tep-down	**S**tep-down	**A**lternating
Ultrafiltration profile	-	Control	PS	NS	NA
			IDH↓, Na gain ↑	No effect	No effect
	+	U	PS+U	NS+U	NA+U
		No effect	IDH↓, Na gain ↑	IDH↓, Na gain ↓	IDH↓, Na gain ↓

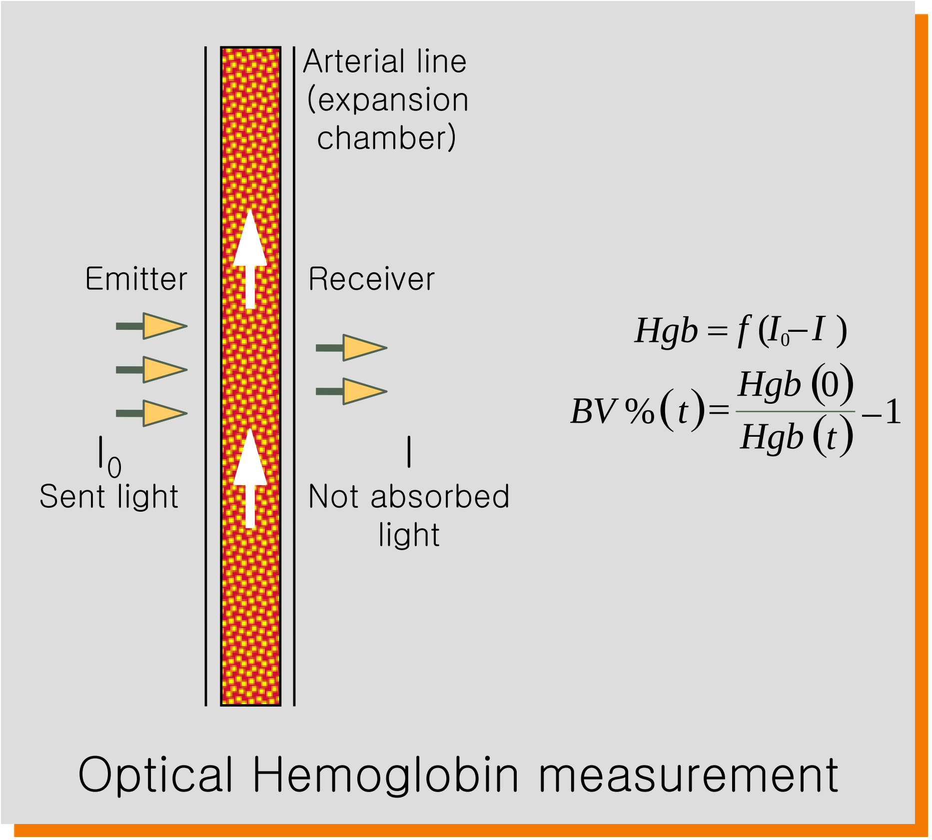
Conclusions)

1) Na balance positive SPHDs is effective but result in Na gain
2) Na balance neutral SPHDs is effective without Na gain
   if UFP is combined

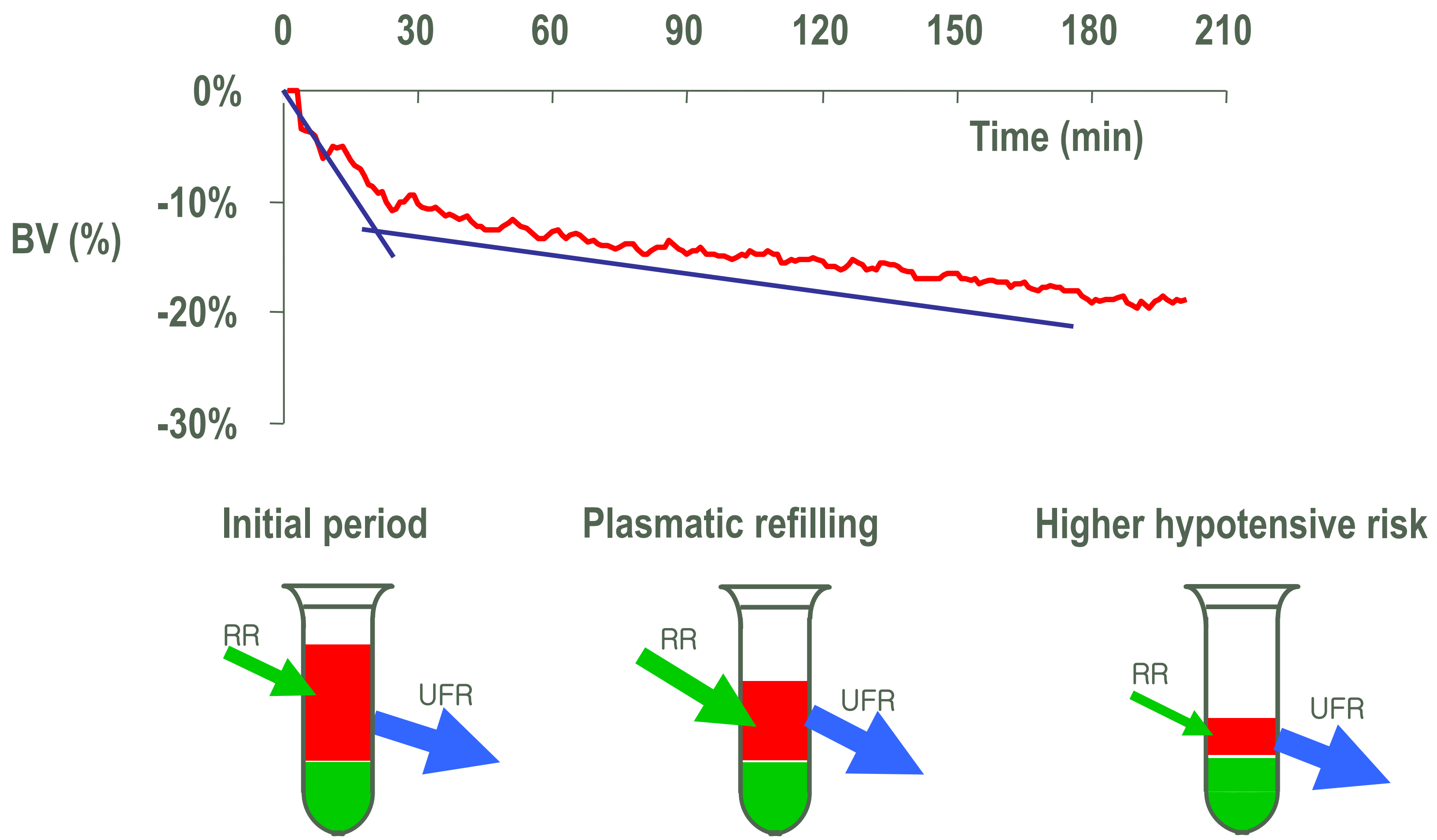
Song JH *JASN* 2005, Vol 16

Principle of Blood Volume Monitor (BVM)

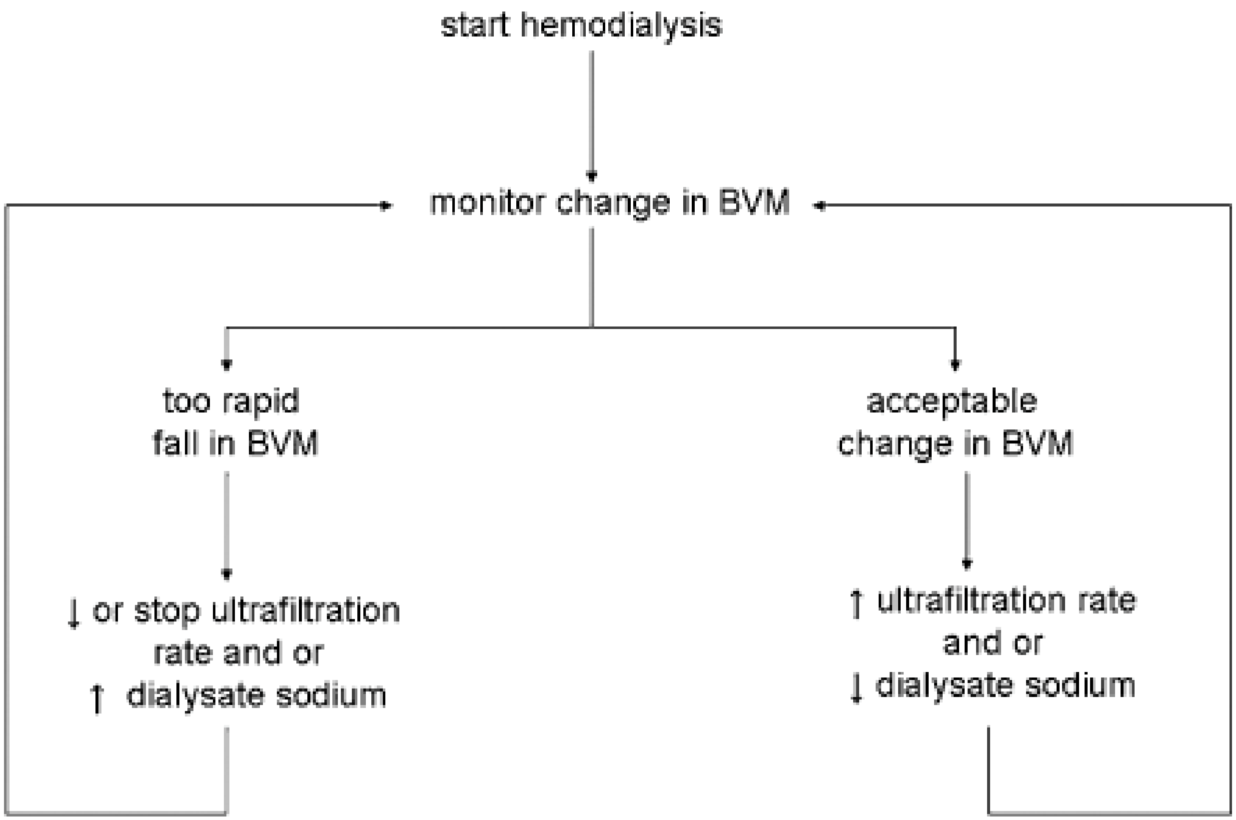




Changes in blood volume during hemodialysis

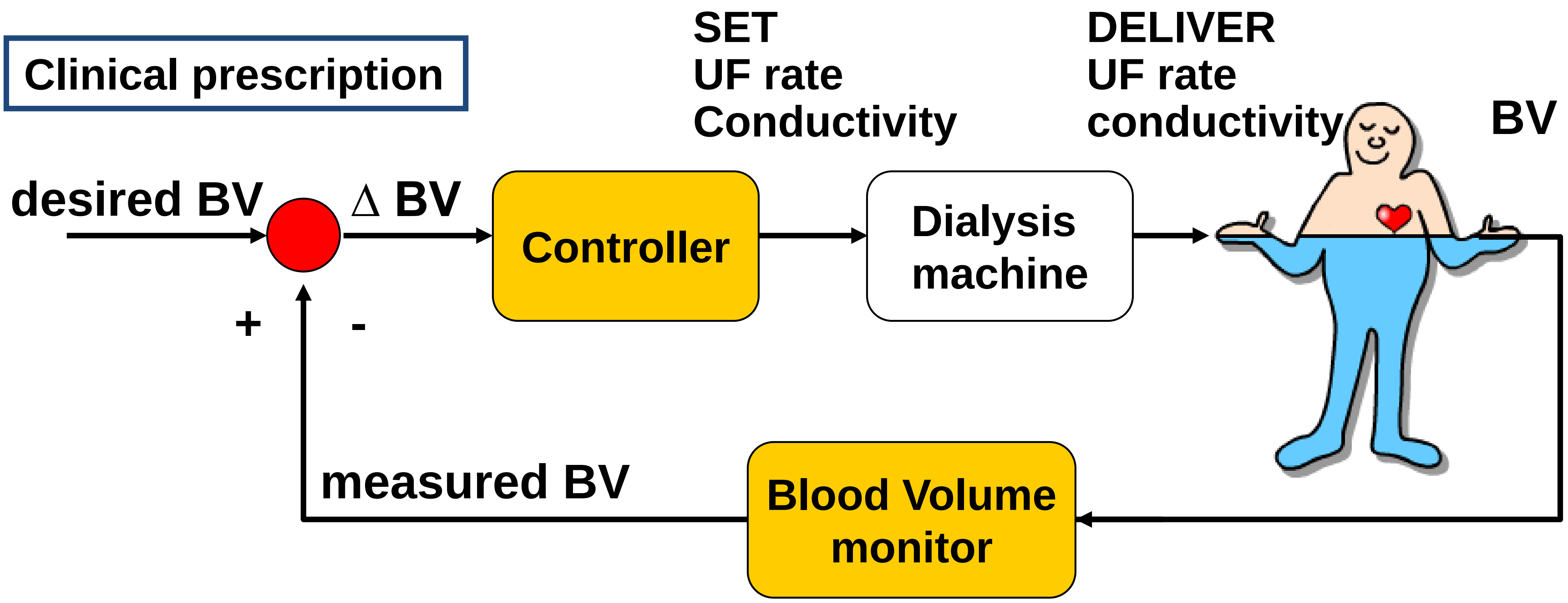


"Fuzzy" logic control system for regulating changes in relative blood volume (BVM).



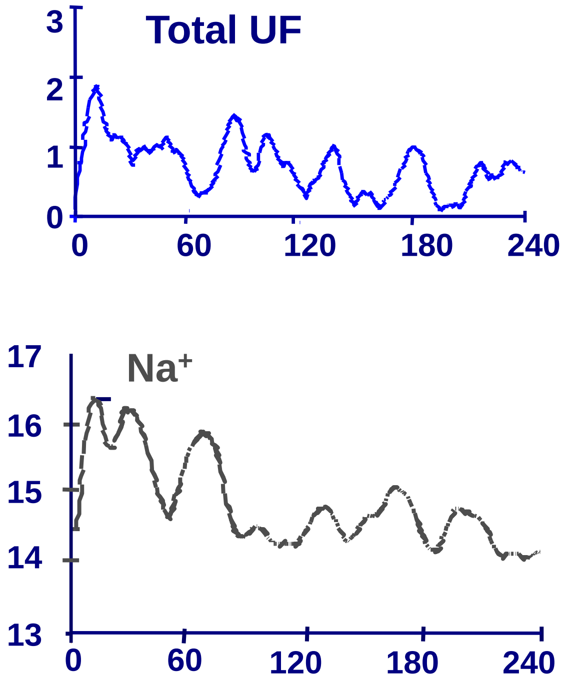
Hemodialysis International 2011 Oct ; 15 : S37-S42

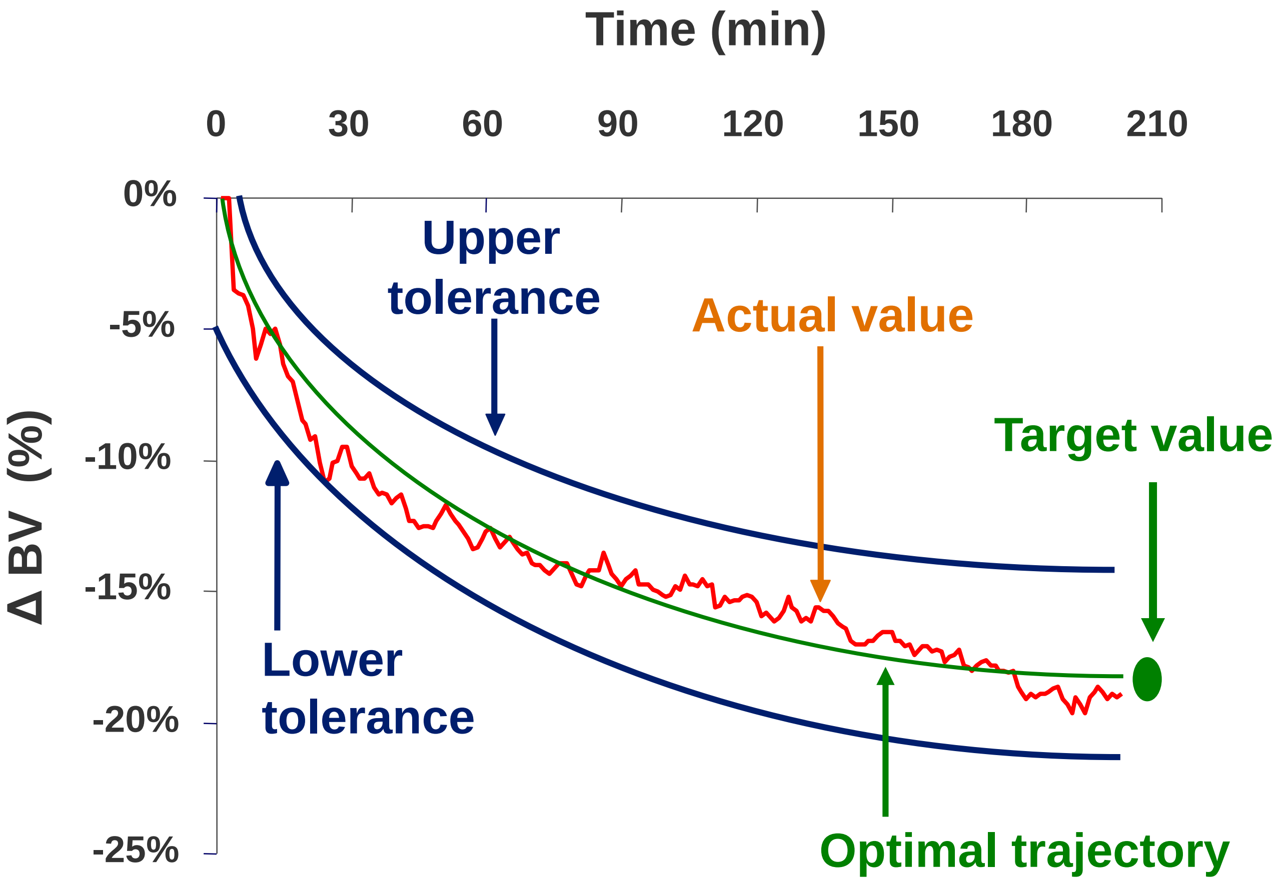
Automated blood volume regulation during hemodialysis (Biofeedback)



measuring + **automated actions**

Leading blood volume along the optimal trajectory

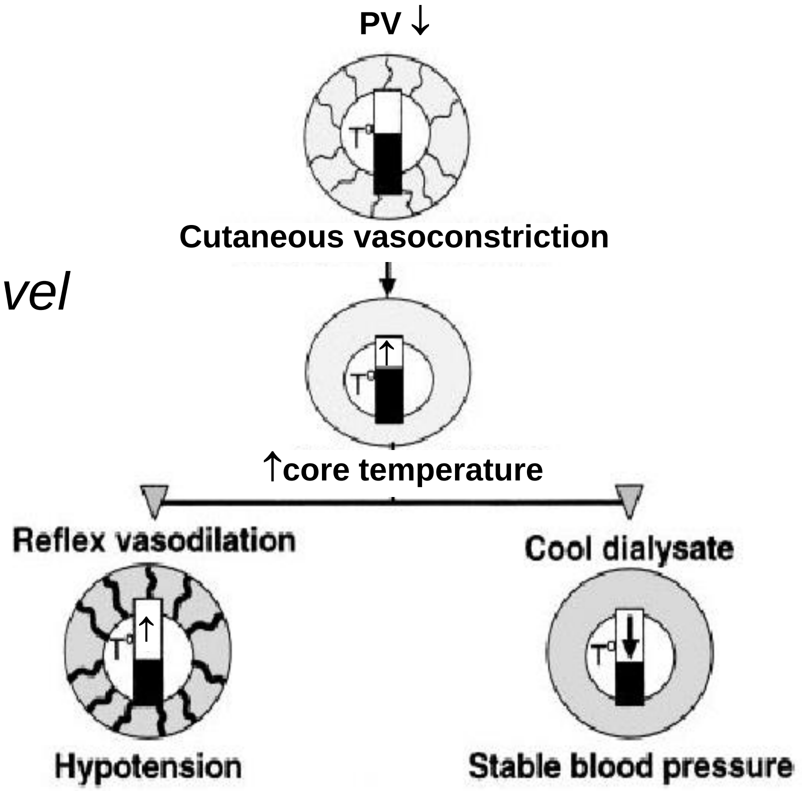




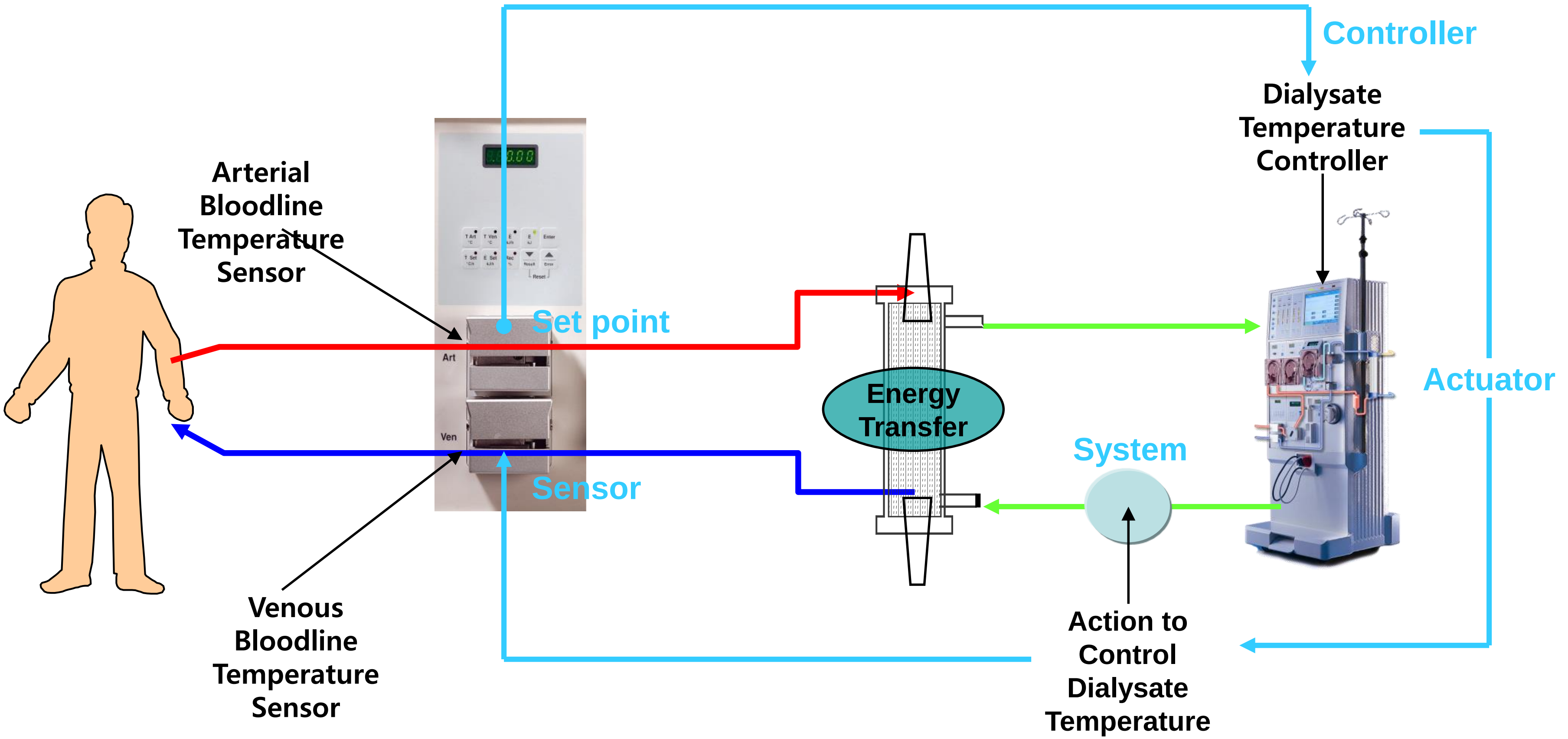
Cold Dialysate

- ↓Plasma volume
  → cutaneous vasoconstriction
  → ↑core temperature
  (impaired thermal balance)
  → peripheral vasodilatation *in critical level*
  → IDH

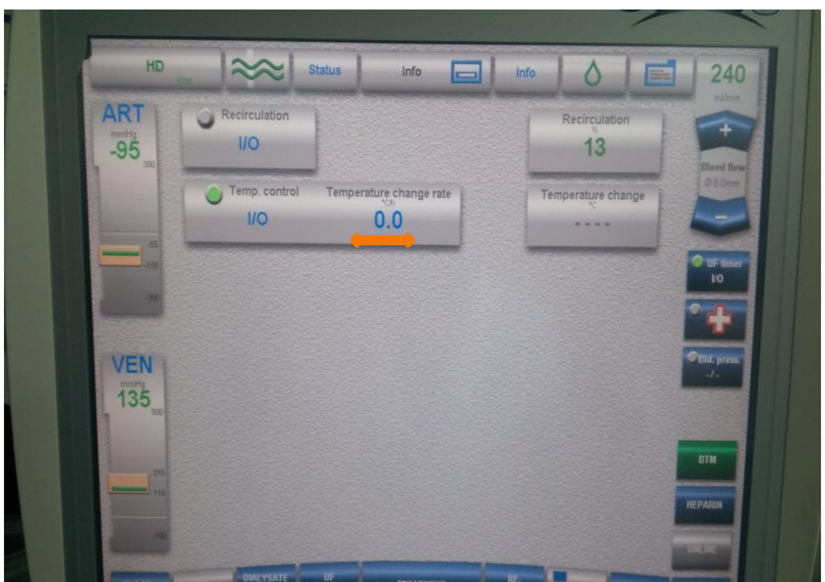
- 36.5 ~ 38 °C → 35~35.5°C : ↓ IDH



Blood Temperature Monitor (BTM)

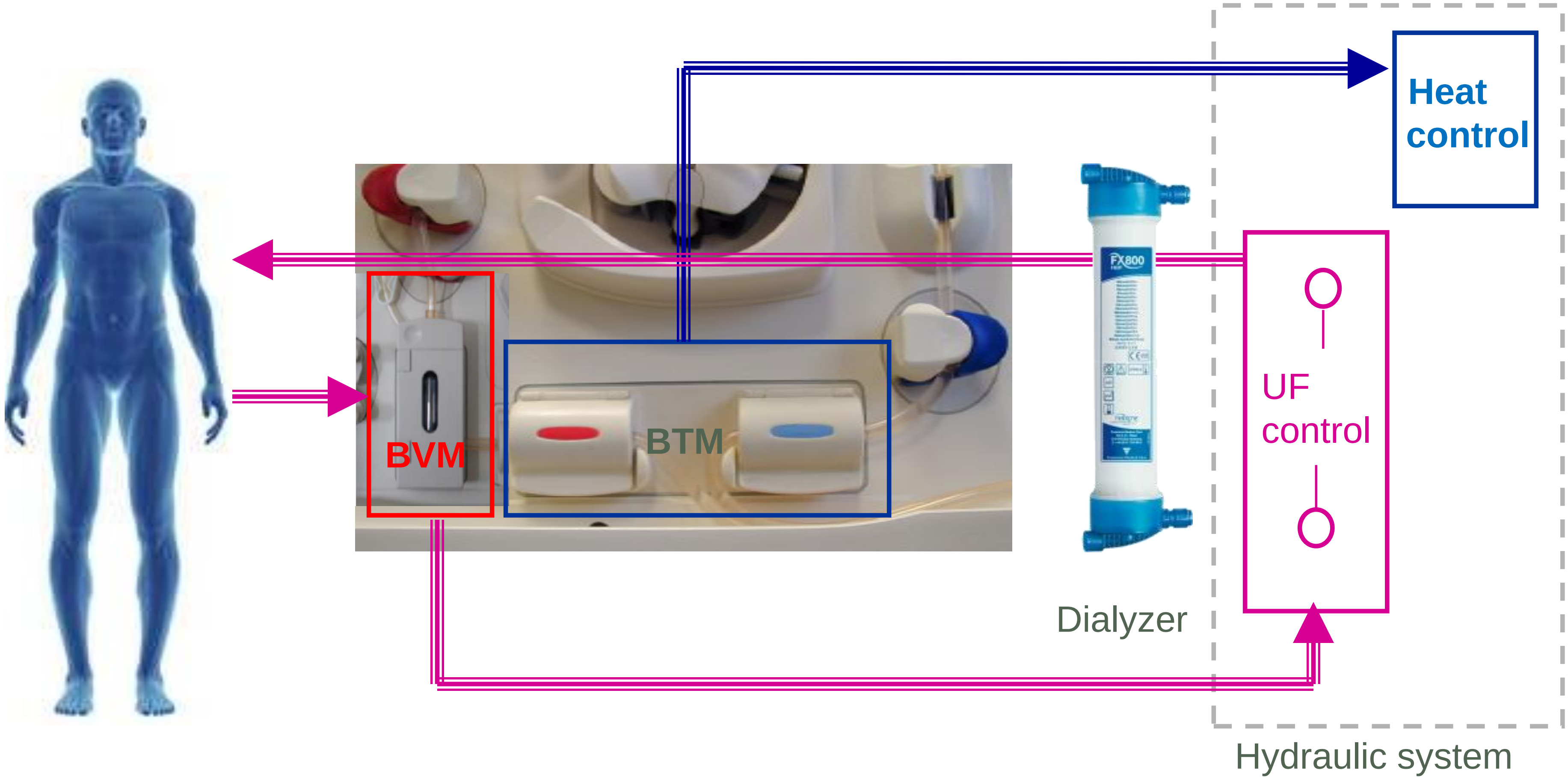


Close-Loop Control System


HD
Status
Info
Info
240
ART
mmHg
-95
Recirculation
I/O
Recirculation
13
Temp. control
I/O
Temperature change rate
0.0
Temperature change
VEN
mmHg
135
UF timer
I/O
Bld. press.
BTM
HEPARIN
TREATMENT


HDF postdilution
Status
Info
280
ART
mmHg
-145
Recirculation
I/O
Recirculation
15
Temp. control
I/O
Temperature change rate
-0.5
Temperature change
-0.2
VEN
mmHg
215
BTM
HEPARIN
ONLINE
TREATMENT
OPTIONS
SYSTEM

BTM & BVM in feedback loop



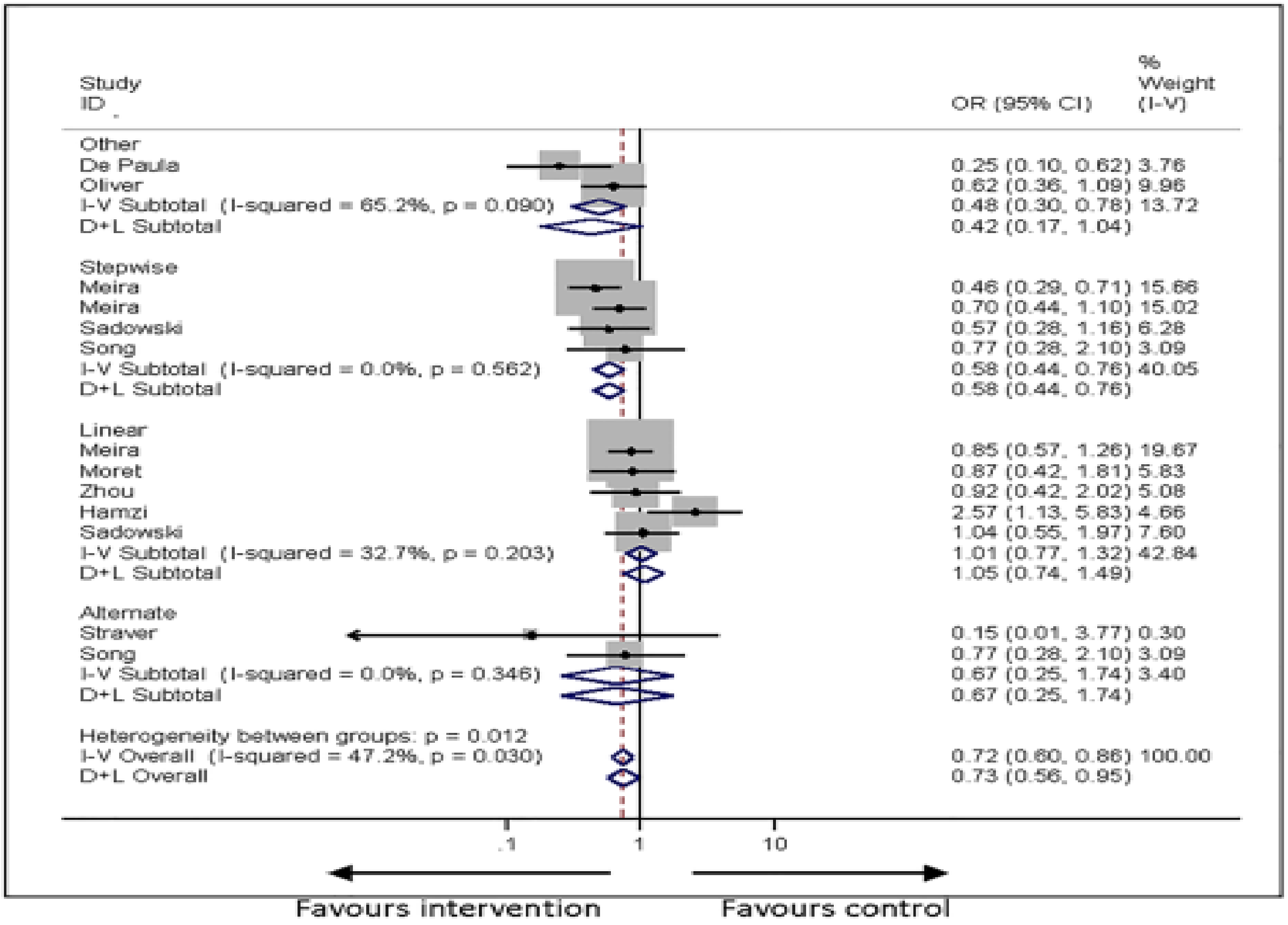
Landmark-Reports of Each Maneuver (profiling HD)

- IDH prone patients (*NDT*, 2006)
  - Control : 25% (16/64) IDH
  - Na profile (LD) : 23% (15/65) IDH
  - UF profile (LD) : 31% (19/61) IDH
  - Na + UF profile (LD) : 10%% (7/73) IDH
- IDH prone patients (*JASN*, 2005)

%	Control	PS	PS+U	NS+U	NA+U
Intradialytic discomfort	51.5	21.2	24.2	24.2	30.3
Interdialytic discomfort	18.2	45.5	36.4	15.2	21.2

- A meta-analysis of sodium profiling techniques (*Hemo Int*, 2017)
  - Stepwise profiling was more effective than other profiling methods
  - Linear profiling had no evidence to be any more effective than conventional HD

A meta-analysis of sodium profiling techniques and the impact on intradialytic hypotension



Hemodialysis International
2017; 21:312-322 DOI: 10.1111/hdi.12488
http://onlinelibrary.wiley.com/doi/10.1111/hdi.12488/full#hdi12488-fig-0003

Landmark-Reports of Each Maneuver (Hemocontrol® or BTM®)

- IDH prone patients (*KI*, 2002) : Hemocontrol® HD
  - Conventional HD vs BVC HD : 30% reduction of IDH in BVC HD
- IDH prone patients (*NDT*, 2006) : Hemocontrol® HD
  - Symptomatic IDH : 8% BVC feedback, 16% standard HD, 14% Na profile HD, 17% DC-controlled feedback
- IDH prone patients (*Plos One*, 2015) : Hemocontrol® HD
  - 2-fold increase in plasma AVP at 30 minutes into biofeedback session

- IDH prone patients (*AJKD*, 2002) : Isothermic feedback
  - Conventional HD vs Isothermic HD : 50% reduction of IDH in Isothermic HD
- 2 RCT (*CJASN*, 2015) ; Programmed cooling to 0.5°C below BT
  - 1 year use can reduce the progression of cardiomyopathy and protect against ischemic brain damage

Clinical benefits in dialysis patients

ORIGINAL ARTICLE
Nephrology

JKMS

http://dx.doi.org/10.3346/jkms.2014.29.6.805 • J Korean Med Sci 2014; 29: 805-810

Efficacy of Hemocontrol Biofeedback System in Intradialytic Hypotension-Prone Hemodialysis Patients

Hyo-Wook Gil,[1] Kitae Bang,[2] So Young Lee,[3] Byoung Geun Han,[4] Jin Kuk Kim,[5] Young Ok Kim,[6] Ho Cheol Song,[7] Young Joo Kwon,[8] and Yong-Soo Kim[9]

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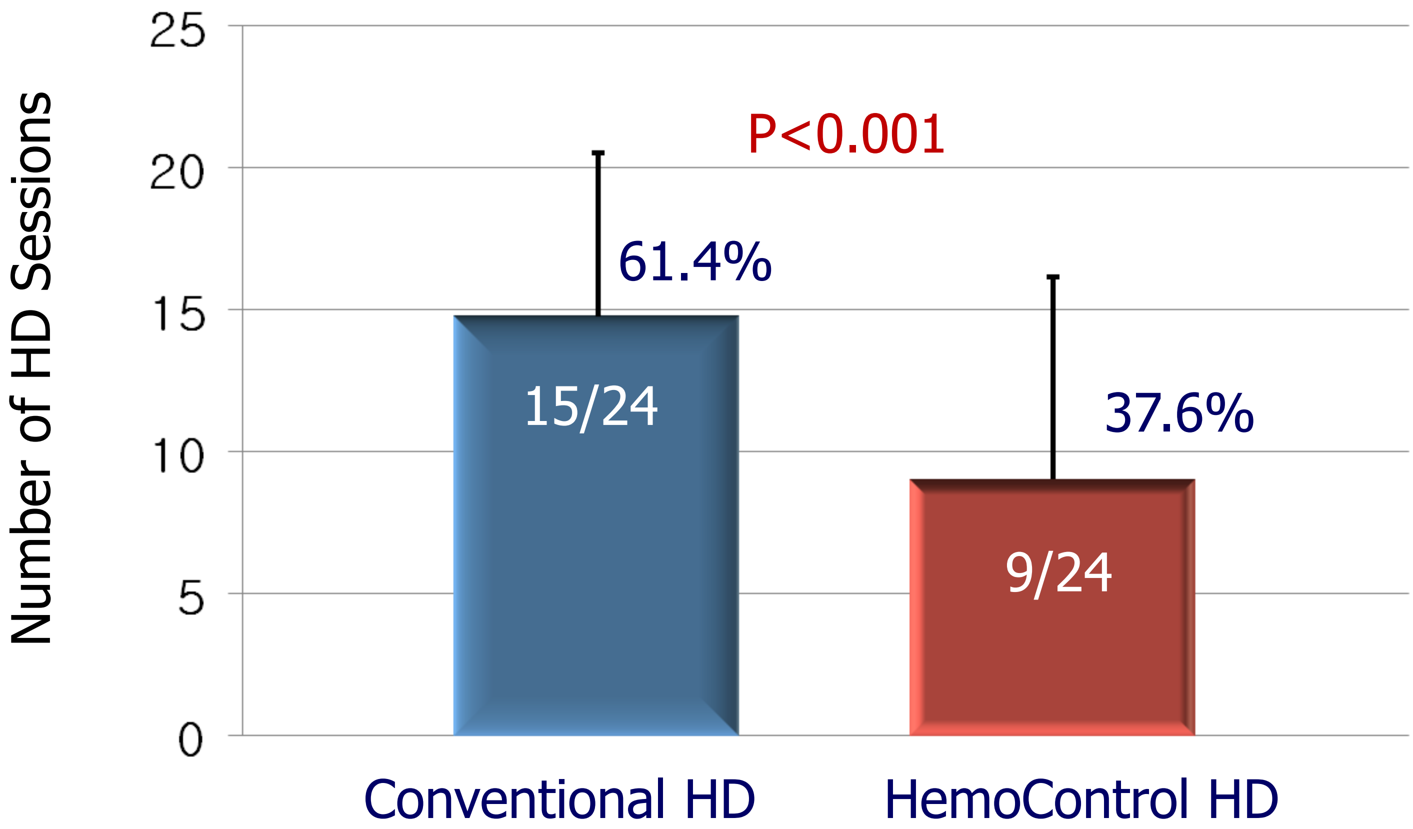
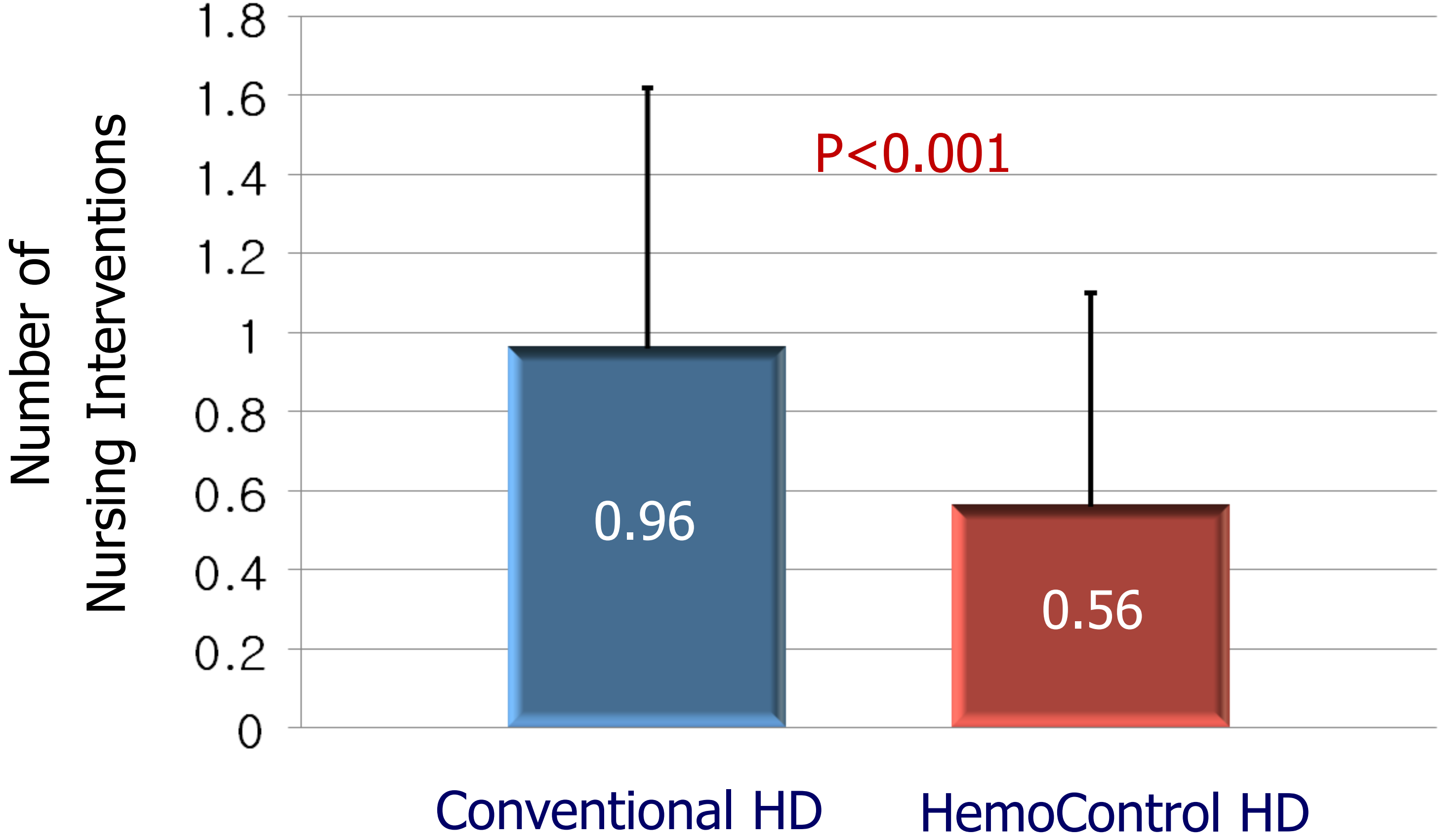
We conducted a study to determine whether the hemocontrol biofeedback system (HBS) can improve intradialytic hypotension (IDH) in hypotension-prone hemodialysis (HD) patients compared with conventional HD. In this multicenter prospective crossover study, 60 hypotension-prone patients were serially treated by conventional HD for 8 weeks (period A), by HD with hemoscan blood volume monitoring for 2 weeks (period B0), and by HBS HD for 8 weeks (period B1). The number of sessions complicated by symptomatic IDH during 24 HD sessions (14.9 ± 5.8 sessions, 62.1% in period A vs 9.2 ± 7.2 sessions, 38.4% in period B1, $P < 0.001$) and the number of IDH-related nursing interventions in a session (0.96 ± 0.66 in period A vs 0.56 ± 0.54 in period B1, $P < 0.001$) significantly decreased in period B1 than in period A. Recovery time from fatigue after dialysis was significantly shorter in period B1 than in period A. The patients with higher post-dialysis blood pressure, lower difference between pre- and post-dialysis blood pressure, less frequent IDH, and higher pre- and post-dialysis body weight in period A responded better to HBS in period B1 in regard to the reduction of IDH. In conclusion, HBS may improve the patient tolerability to HD by reducing the IDH frequency and promoting faster recovery from fatigue after dialysis.

Keywords: Hypotension; Renal Dialysis; Clinical Trial; Dialysis Volume

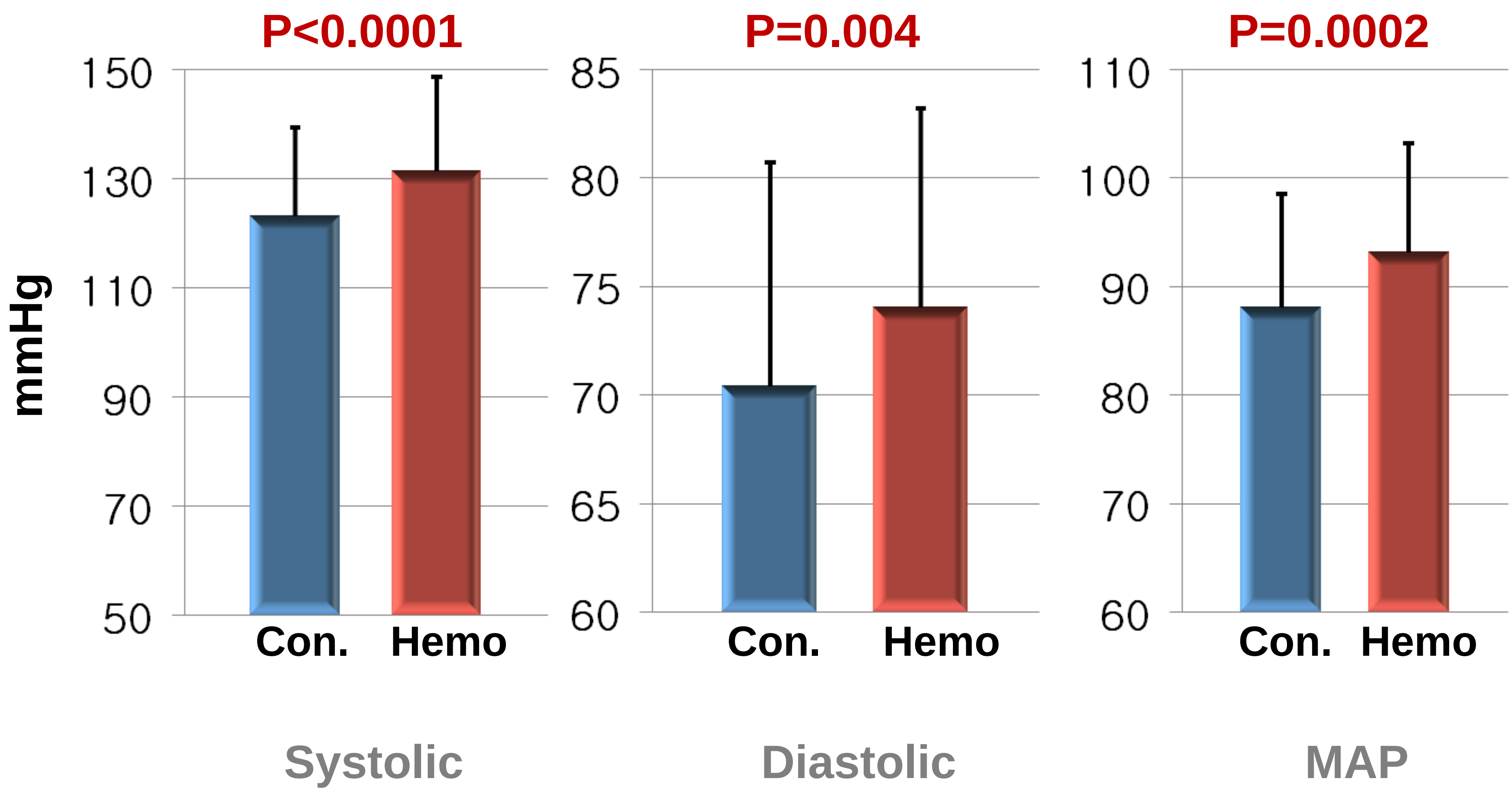
Number of sessions IDH occurred during 24 sessions



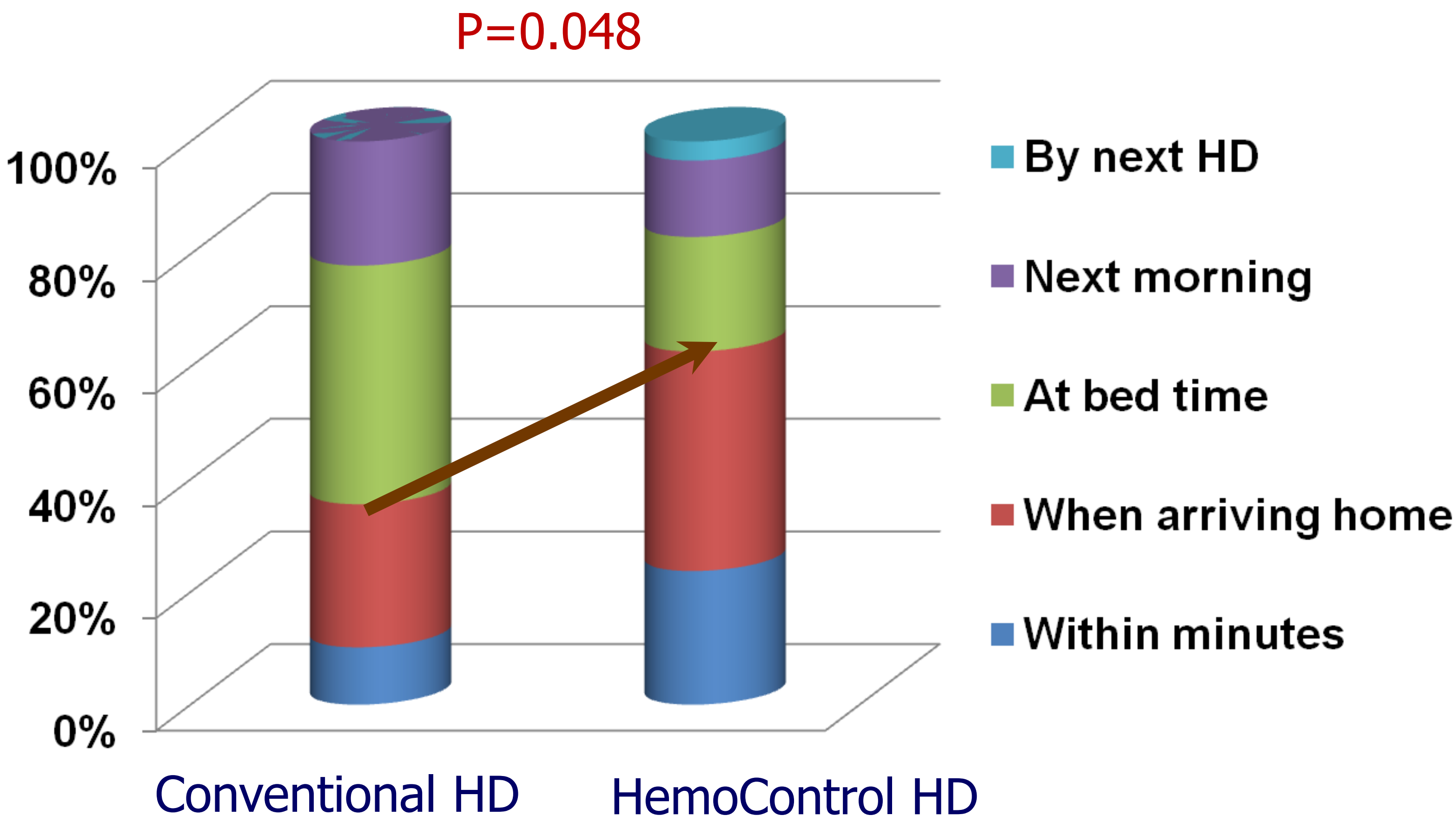
Number of nursing interventions per session



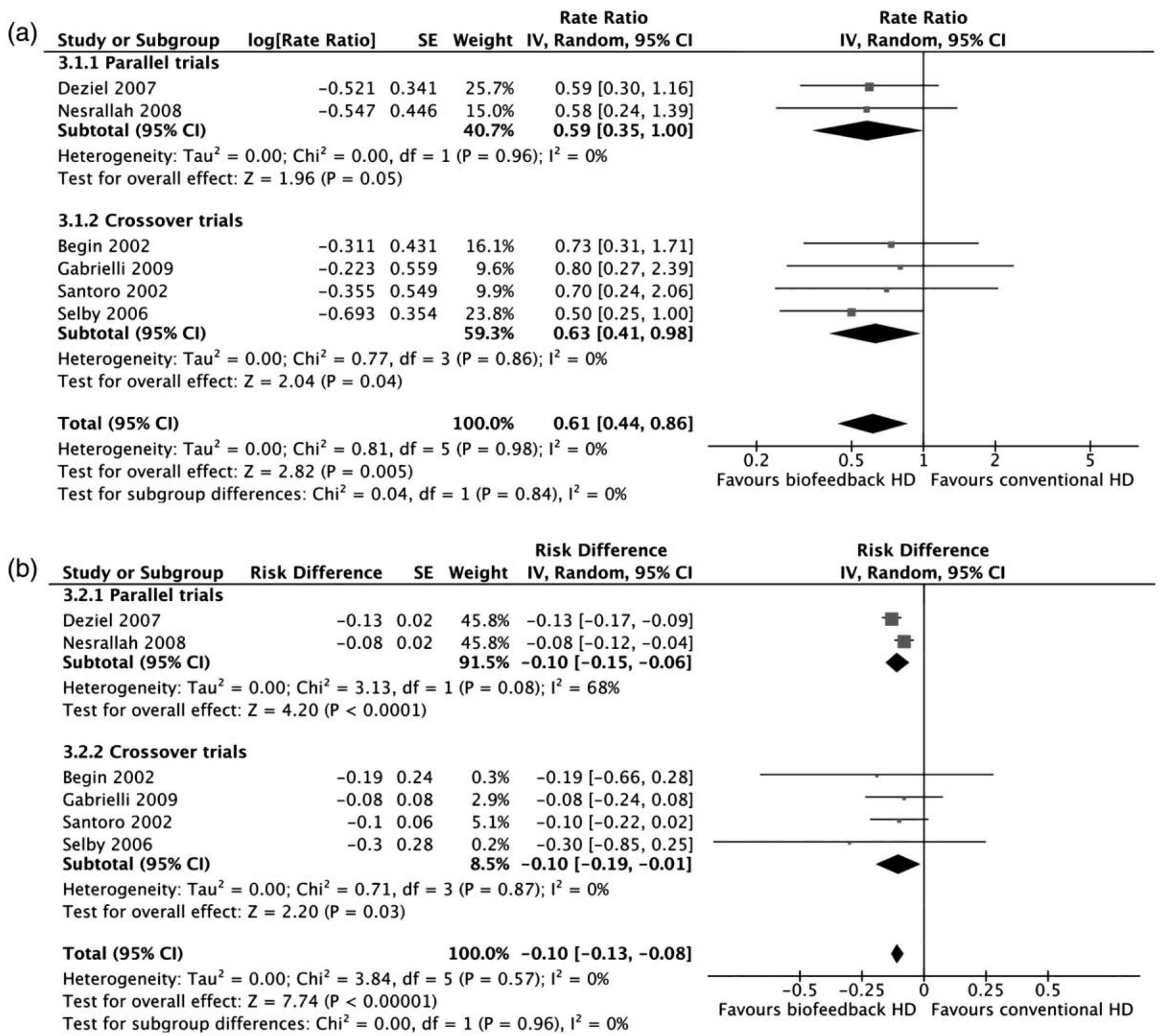
Post-dialysis BP



Recovery of Fatigue After Dialysis



(a) Biofeedback HD versus conventional HD with constant dialysate conductivity and ultrafiltration rate; outcome: IDH. Relative treatment effect estimate (rate ratio).

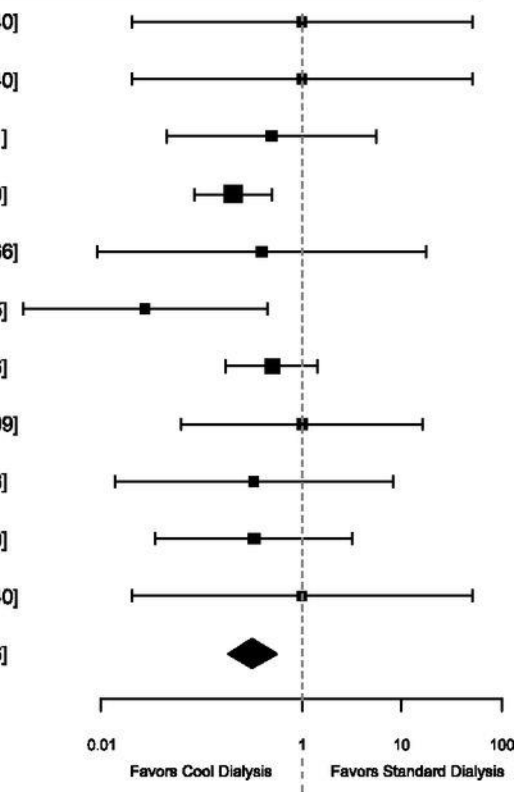


Gihad E. Nesrallah et al. *Nephrol. Dial. Transplant*. 2013;28:182-191

NDT Nephrology Dialysis Transplantation

Effect of low temperature dialysis on intradialytic hypotension. 95% CI, 95% confidence interval; BTM, biofeedback temperature monitoring.

Source	Intervention	Cool Dialysis n / N	Standard Dialysis n / N	Rate Ratio (95% CI)
Ayoub 2004	Fixed 35 C	0 / 30	0 / 30	1.00 [0.02, 50.40]
Beerenhout 2004a	BTM 35.2 C	0 / 12	0 / 12	1.00 [0.02, 50.40]
Chesterton 2009	Fixed 35 C	1 / 9	2 / 9	0.50 [0.05, 5.51]
Cruz 1999	Fixed 35.5 C	6 / 99	29 / 99	0.21 [0.09, 0.50]
Dheenan 2001	Fixed 35 C	0.375 / 30	0.937 / 30	0.40 [0.01, 17.66]
Jost 1993	Fixed 35 C	0 / 12	18 / 12	0.03 [0.01, 0.45]
Kaufman 1998	BTM 35.7 C	5 / 15	10 / 15	0.50 [0.17, 1.46]
Selby 2006	Fixed 35 C	1 / 9	1 / 9	1.00 [0.06, 15.99]
van der Sande 1999	Fixed 35.5 C	0 / 9	1 / 9	0.33 [0.01, 8.18]
van der Sande 2009	BTM 0.5C below body temperature	1 / 21	3 / 21	0.33 [0.03, 3.20]
Yu 1995	Fixed 35 C	0 / 18	0 / 18	1.00 [0.02, 50.40]
Total				0.32 [0.18, 0.56]

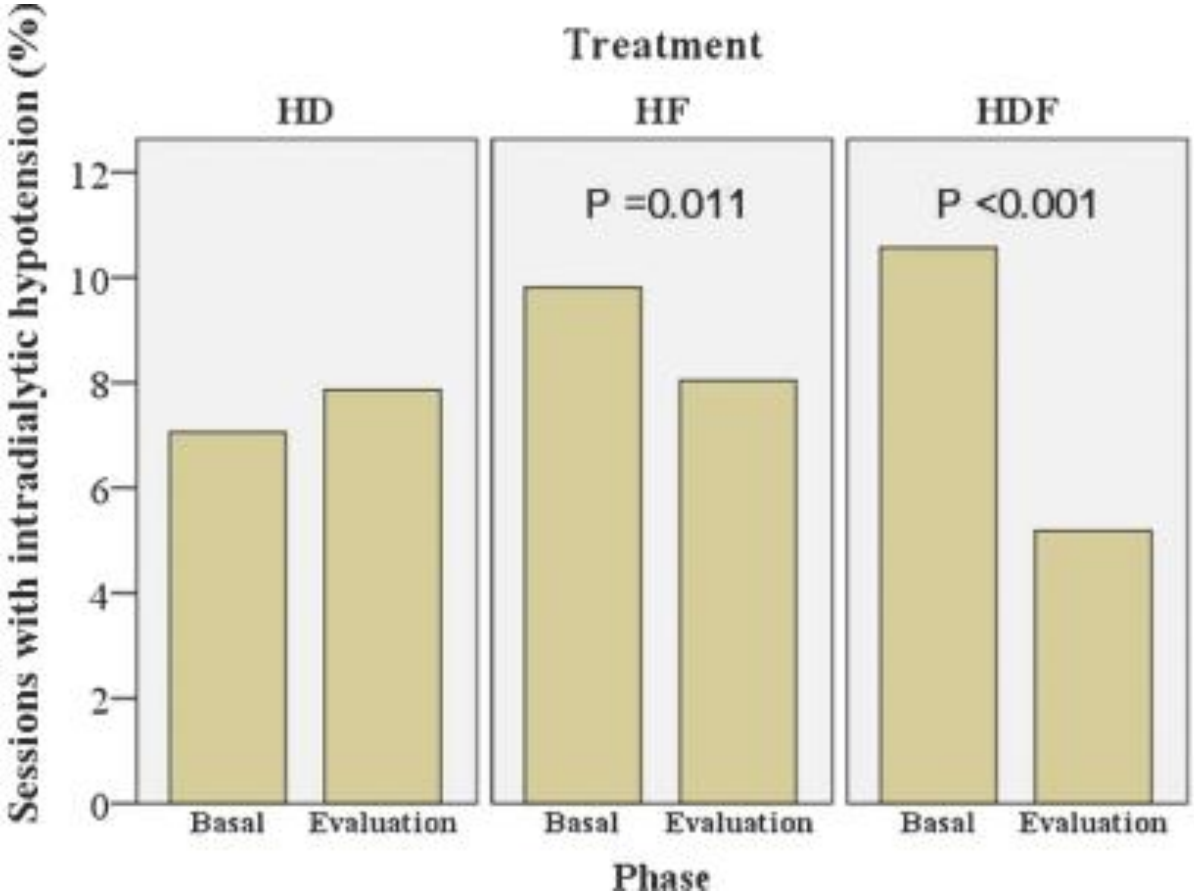


Test for heterogeneity for pooled Rate Ratio: $Chi^2 = 6.35$, $df = 10$ ($P=0.78$), $I^2=0\%$

Reem A. Mustafa et al. *CJASN* 2016;11:442-457

CJASN

Hemofiltration and Hemodiafiltration Reduce Intradialytic Hypotension in ESRD (RCT)



Locatelli et al, *JASN* 2010 Oct; Vol 21

Take Home Messages

- All these developments have not been able to totally abolish hypotension
- Unlikely any single successful treatment option exists, but rather an integrated, multidisciplinary approach may need : Biofeedback technologic combination (Hemocontrol® plus BTM®)
- To create an individual patient dialysis profile may prove more successful
- Attention needs to reduce interdialytic weight gains, so reducing UF requirements : technology can not alone compensate for excessive weight gains
- Ultimately, these maneuvers need to demonstrate a mortality and morbidity benefit