# Real Facts About Fluid Overload

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## Disclosure

- None

## Objectives

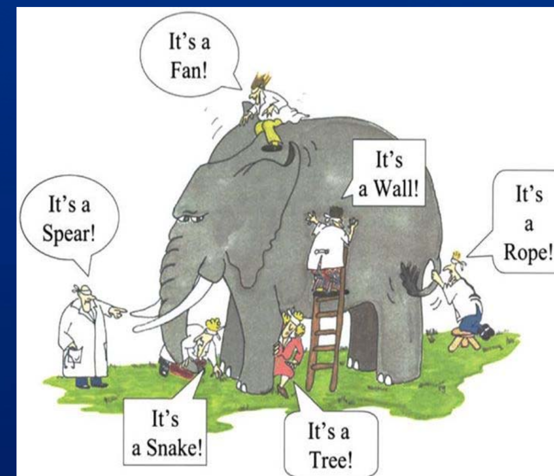
Discuss the meaning of fluid overload and its negative physiological effects on the body of a person who has kidney failure.

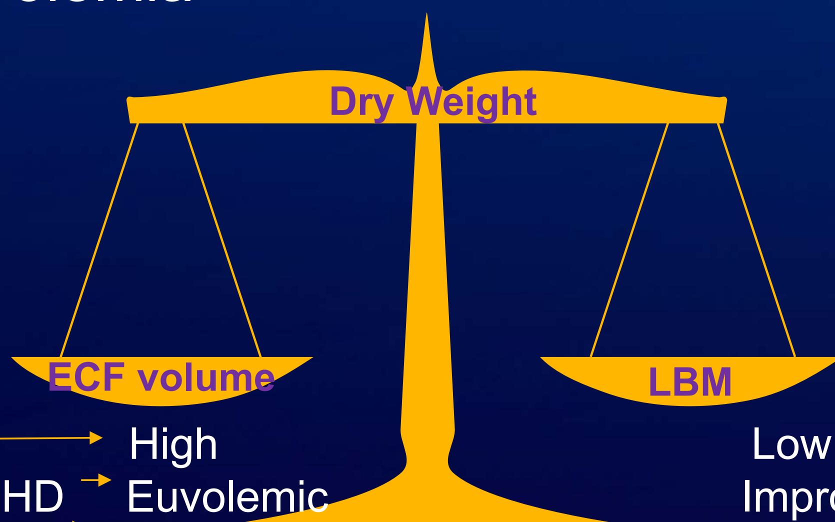
# Two major functions of dialysis

| | **Uremic solute removal** | **Excess ECF volume removal** |
|---|---|---|
| Main Process | Diffusion | Ultrafiltration |
| How is adequacy measured? | Clearance of surrogate solute - urea | BP control, Dry weight |
| Quantification of adequacy | spKt/V, Std Kt/V, URR | No objective measure to quantify adequacy of fluid removal. Trial & Error method to achieve DW |
| Debate | Small versus middle molecular clearance (diffusive versus Convective clearance) | What is the best method to quantify ECF volume removal. Clinical versus Non-clinical methods |

# What is dry weight?

- Lowest tolerated post-dialysis weight achieved via a gradual reduction in post dialysis weight at which there are minimal signs or symptoms of hypovolemia or hypervolemia




| | ECF volume | LBM |
|---|---|---|
| Initiation of HD → | High | Low |
| Adequate Maintenance HD → | Euvolemic | Improves |
| Acute illness → | Increases | Decreases |

# Negative Effects of Fluid Overload ("Volutrauma")

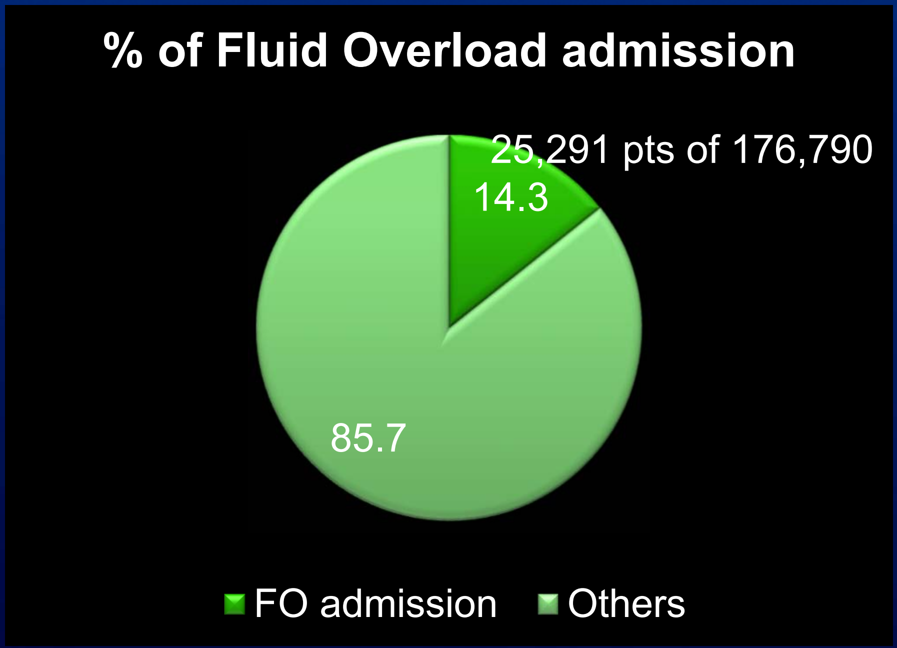
Acute Fluid Overload

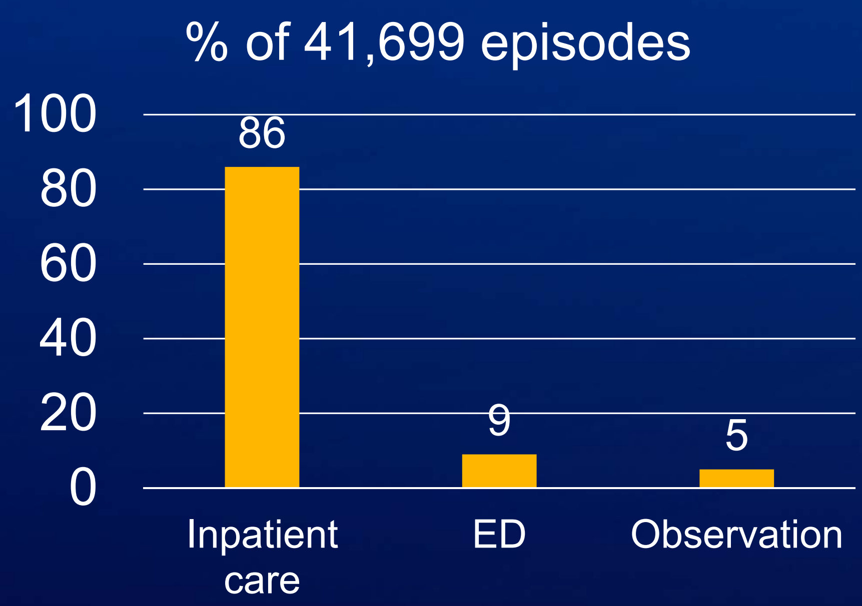
- Dyspnea
- CHF
- Hospitalization

Chronic Fluid Overload

- Hypertension
- LVH
- CHF
- Decreased vascular compliance
- Increased cardiovascular mortality
- Organ dysfunction
  - Gut edema: malabsorption
  - Tissue edema: poor wound healing
  - Renal edema: renal BF, reduced GFR
  - Pulmonary edema

# Cost of Hospitalization for Volume Overload



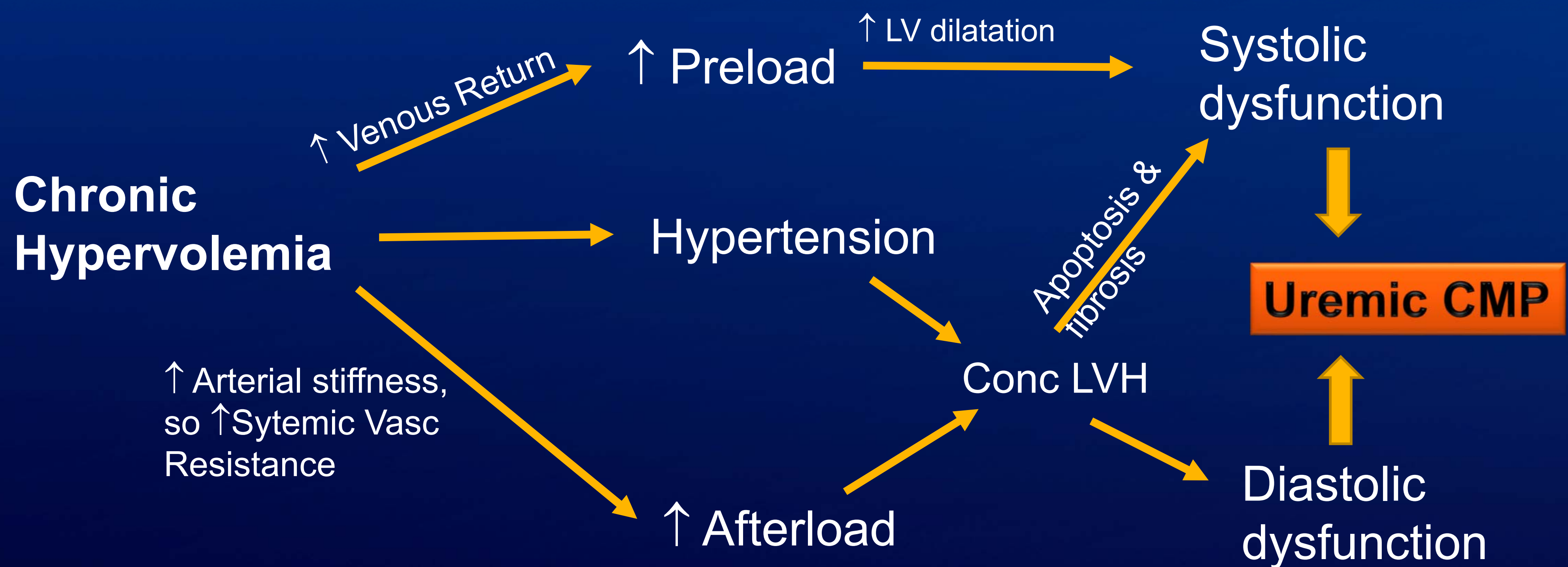




Average cost per episode **$6,372**

Total cost **$266 million**

- *Arneson et al. CJASN 2010; 5(6): 1054 – 1063*

# Pathophysiology of Volutrauma



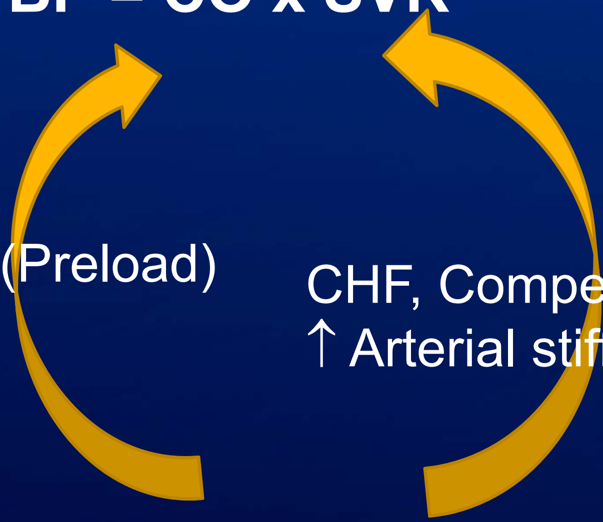
# Fluid Overload and Hypertension

DOPPS: Frequency of hypertension (pre-dialysis SBP > 140): 60 – 70%

*Dialysis Outcomes and Practice Patterns Study www.dopps.org*

# How does Fluid Overload cause hypertension?

**BP = CO x SVR**



↑ VR (Preload)

CHF, Compensatory neurohormonal activation
↑ Arterial stiffness

**Volume overload or Fluid overload**

70 – 80% of hypertension in dialysis is from volume excess, 20 -30% other causes

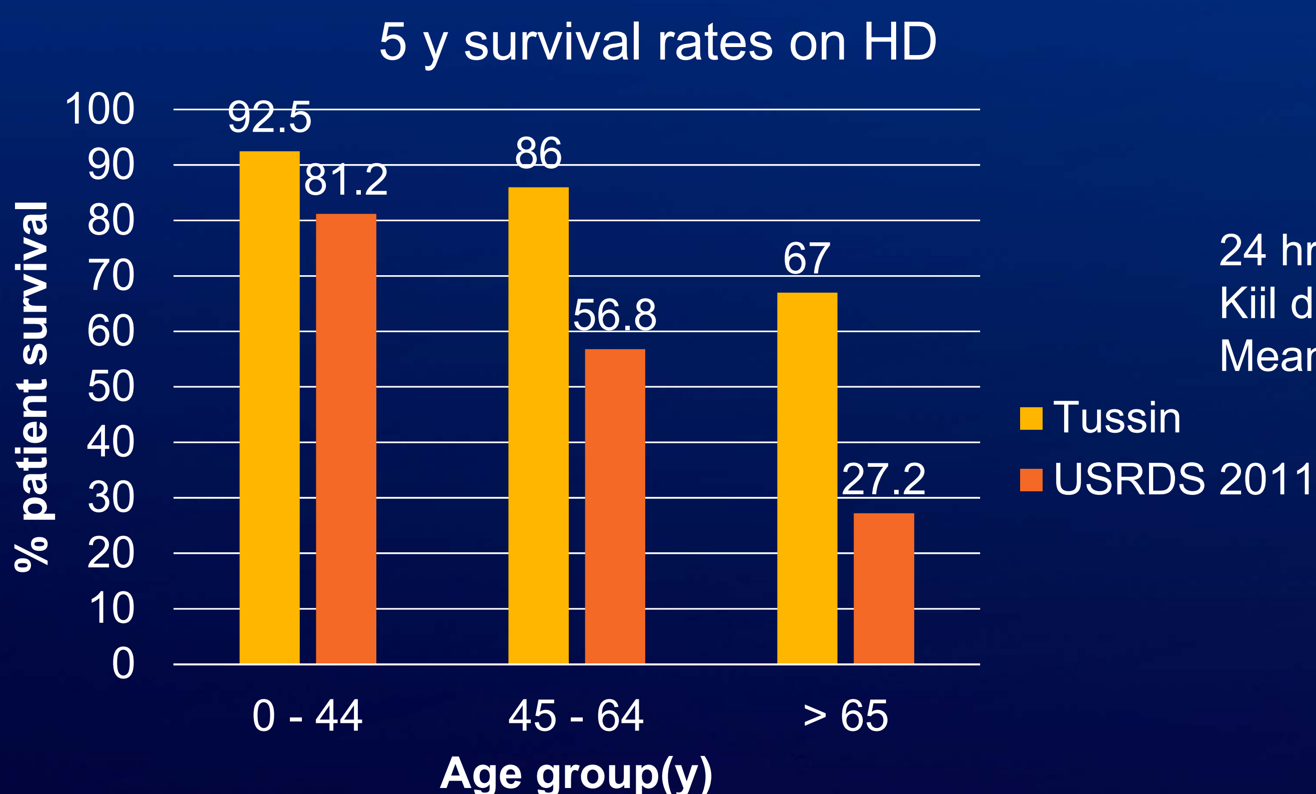
# IF Fluid Overload causes HTN then Excess volume removal should reduce BP: Proof?

- Several observational studies have shown that reducing DW improves BP control
- Two centers practicing strict volume control have 2 – 4 % hypertension prevalence
  - Tassin, France
  - Ege University, Izmir, Turkey
- DRIP trial
- FHN trials

# Survival as an index of adequacy of dialysis

BERNARD CHARRA, EDOUARD CALEMARD, MARTIAL RUFFET, CHARLES CHAZOT, JEAN-CLAUDE TERRAT, THIERRY VANEL, and GUY LAURENT

*Centre de rein artificiel, Tassin, France*




24 hrs/week HD,
Kiil dialyzers
Mean spKT/V 1.7

Kidney International, 1992; 41: 1286 - 1291

# Editorial: Belding H. Scribner

- “Shortly after our first patient, Mr. Clyde Shields, began long term hemodialysis in March of 1960, he developed malignant hypertension, and death seemed imminent . Since we were unable to control his blood pressure with the few antihypertensive drugs then available, we decided that our only hope of saving him was to try aggressive removal of extracellular fluid by ultrafiltration during his once weekly 24-hour hemodialysis.”
- “During the subsequent weeks cramping was severe as we tried to maximize fluid removal during each dialysis. Gradually, however, his blood pressure came under control. Eventually he became normotensive off medication, and remained so until his death from a myocardial infarction in 1971. This dramatic episode made a lasting impression on our approach to the control of blood pressure in our hemodialysis patients.”

# DW Reduction in HTN HD Patients (DRIP Trial)

150 chronic stable HD pts
Avg 2.6 antihypertensives
Uncontrolled HTN (44h interdialytic ABPM)

Intervention group
Progressive reduction in DW by 0.2 kg each HD

Control group
Prescribed DW unchanged

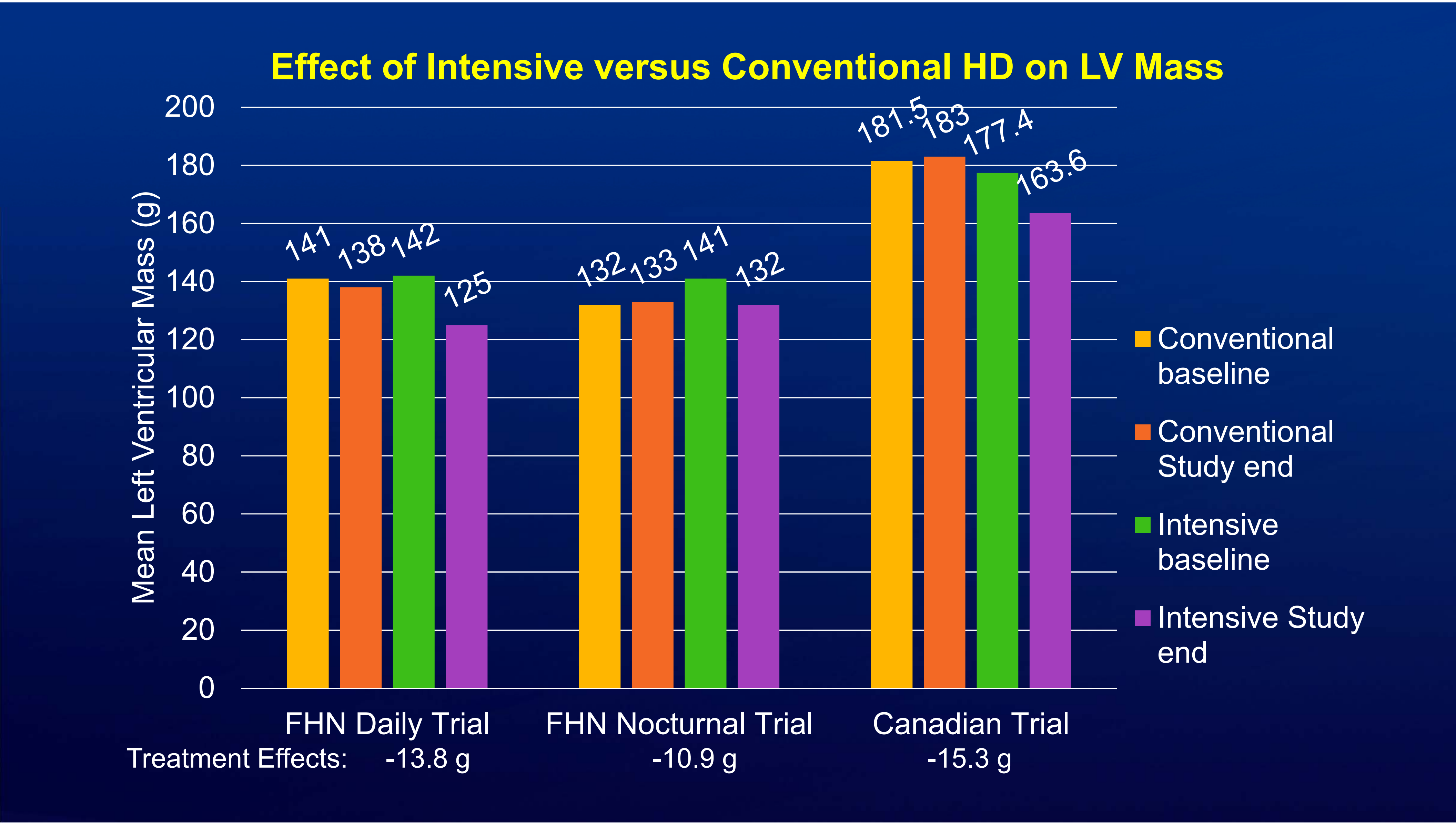
**8 weeks trial:**
**Intervention group weighed 1 kg lower on an average and average reduction in 44h ABPM was 6.6/3/3 mm Hg**

# Fluid Overload and LVH

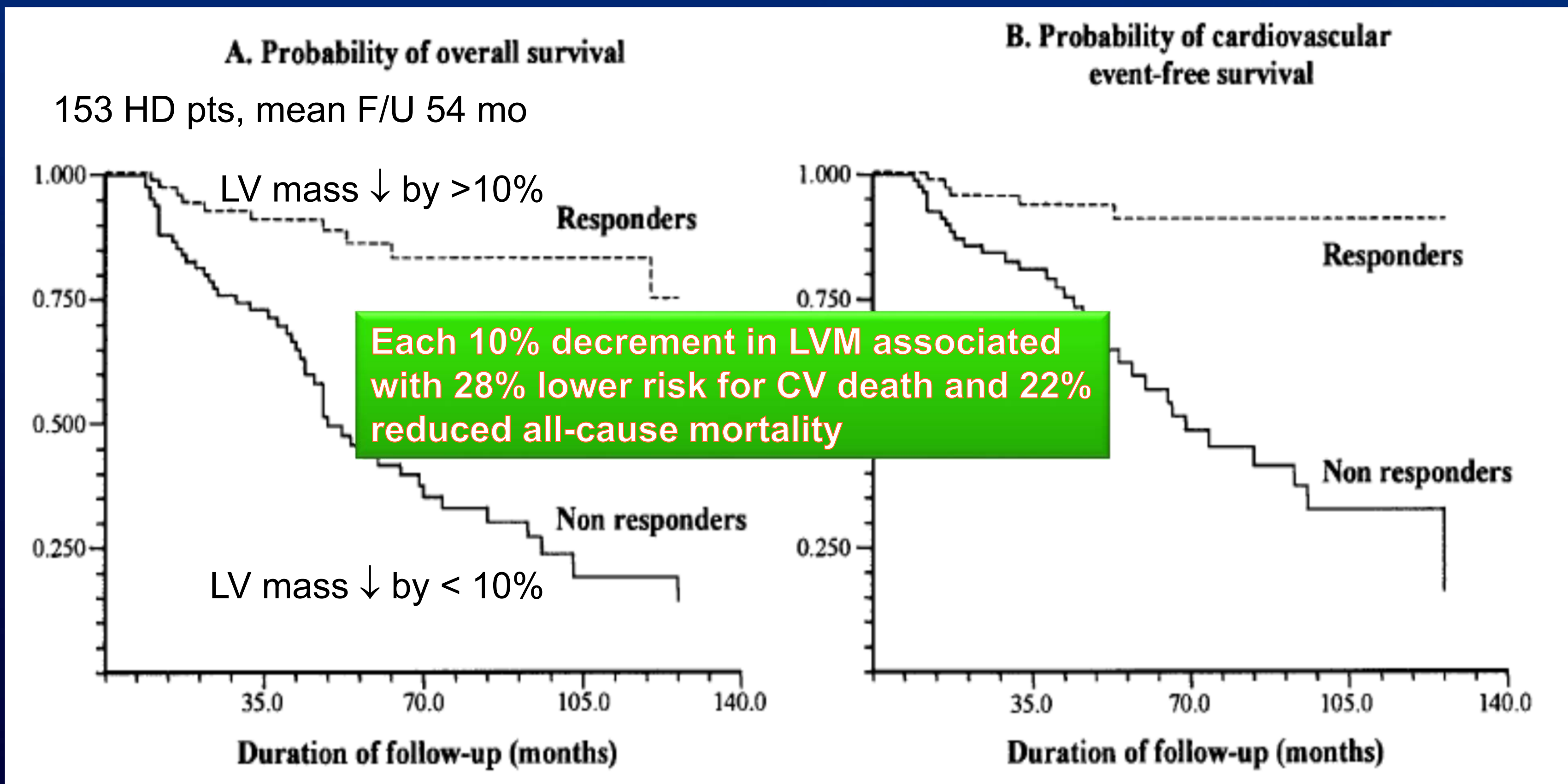
# Volume overload and LVH


**Proof that volume control by dialysis regresses LVH**

No long term trails showing equivocally that volume control leads to consistent reduction in LVMI translating into improved outcomes

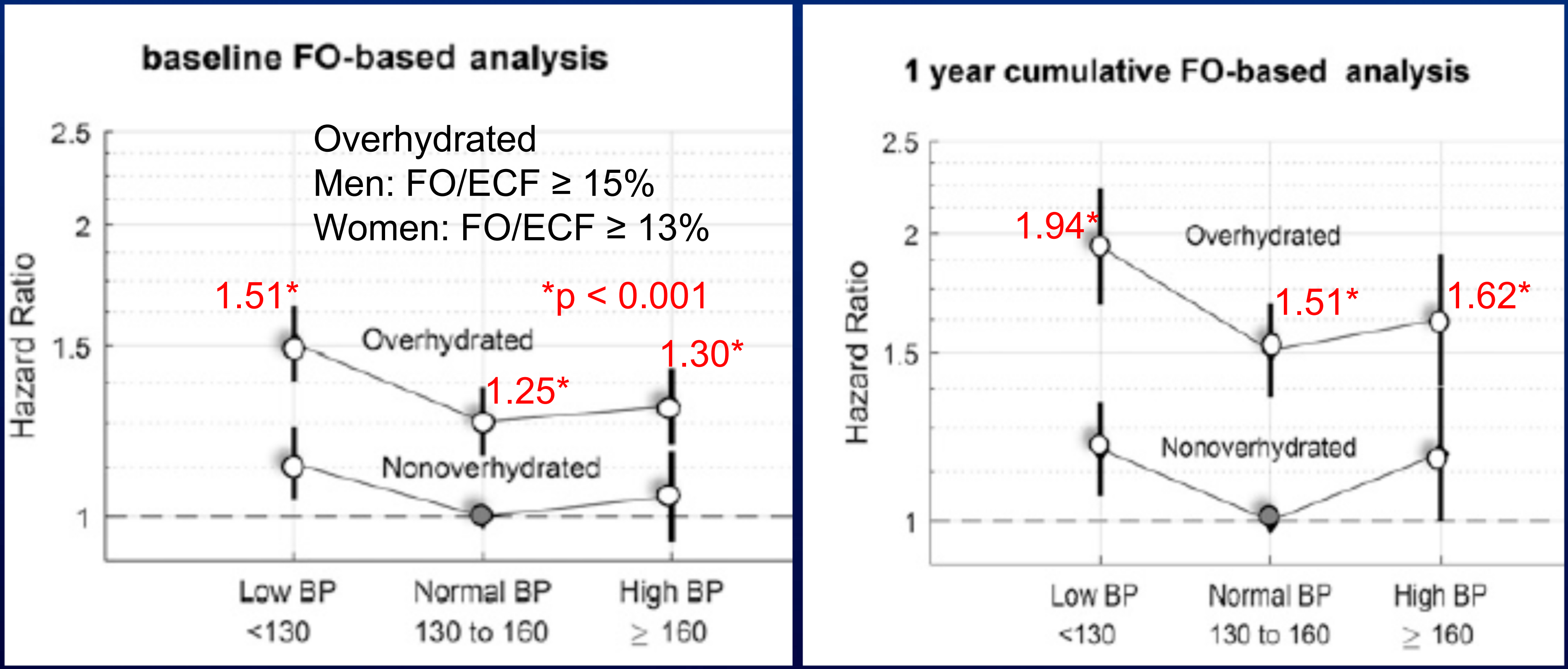

Effect of Intensive versus Conventional HD on LV Mass
Mean Left Ventricular Mass (g)
200
180
160
140
120
100
80
60
40
20
0
141
138
142
125
132
133
141
132
181.5
183
177.4
163.6
Conventional baseline
Conventional Study end
Intensive baseline
Intensive Study end
FHN Daily Trial
FHN Nocturnal Trial
Canadian Trial
Treatment Effects:
-13.8 g
-10.9 g
-15.3 g

# Does regression of LVH lead to improved survival?



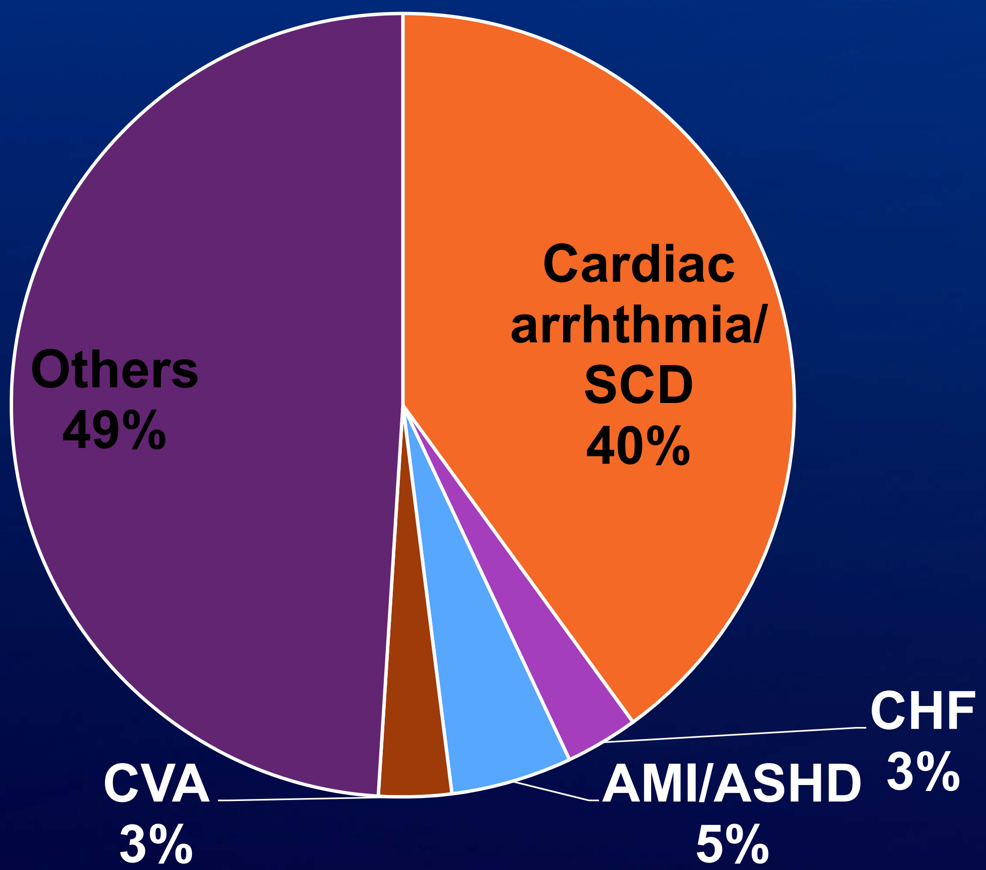

London etal. JASN 2001; 12:2759 – 2767

# Chronic Fluid Overload and Mortality in ESRD: JASN 2017; 28: 2491 - 2497



## Mortality rates 2015, USRDS

ECF volume excess
CKD-MBD, FGF-23
Reduced vascular compliance, increased PW velocity and PP
LVH
Silent ischemia, decreased coronary flow reserve, impaired microcirculation
myocardial stunning
IDH
Higher prevalence of CAD, DM
Ineffective vasoregulation



Why do dialysis patients get Fluid Overloaded?

# Causes of Fluid Overload

**Patient factors**

- Excess sodium intake trumps over fluid intake. Beware of "hidden" salt in processed foods
- Patient reluctance to ↑ Td or frequency or reduce salt intake
- Excessive FRR (↑ IDWG) leading to patient intolerance
- Cardiomyopathy

**Dialysis Process & Facility**

- Short dialysis pattern: Focus on "adequacy of urea removal"
- IDH: UFR > Plasma refill rate
- Inconsistent reimbursement for additional dialysis
- "Asking the patient" How much fluid should we remove?

**Provider Factors**

- Absence of widely available validated tool for DW assessment
- Limited assessment of fluid status
- Limited provision of dietary counseling (low salt intake)
- Delay in adjusting dialysis prescription

# Management of Volume on Dialysis

Assessment of Volume Status

Safe removal of excess fluid

# Assessment of Volume status: Clinical Assessment

**Clinical (Subjective) Assessment**

- Nursing and care provider assessment to be done at each session
- History: Dyspnea, Orthopnea, PND, H/O volume depletion fever, Diarrhea
- Leg edema, sacral edema, puffiness of face
- Raised JVP
- Crackles on lung auscultation, Chest X-ray

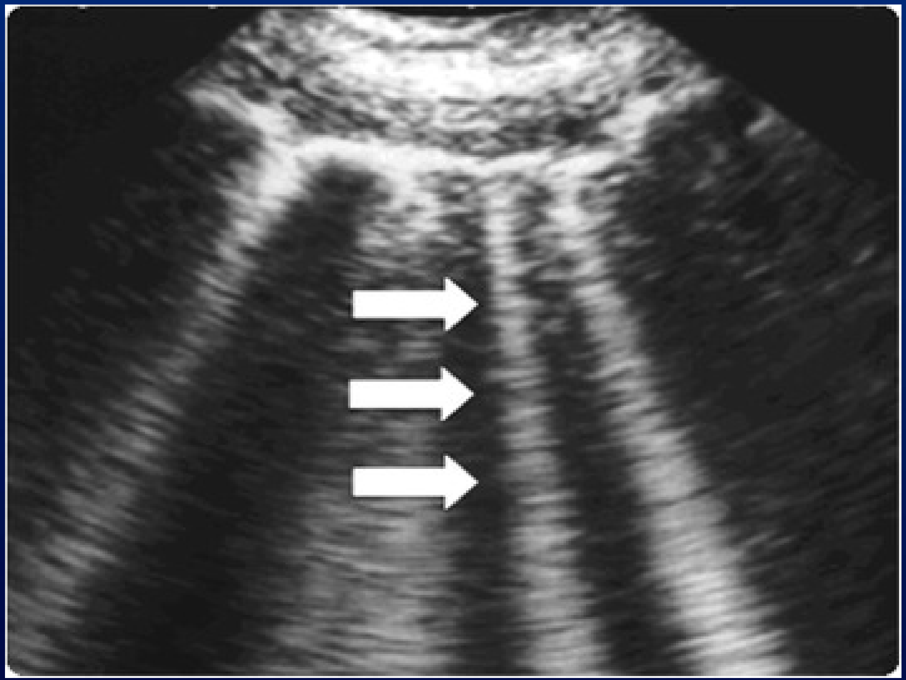
- Pitfalls
  - Clinical skills varies. Poor sensitivity
  - About 1L of interstitial fluid needs to accumulate before peripheral edema becomes evident
  - Other causes: Hypothyroidism, Meds …..

# Assessment of Volume status: Objective Assessment

**Objective assessment tools**

- Invasive: PCWP
- Ultrasound
  - US Lungs
  - Extent of IVC inspiratory collapse
- Bioimpedance analysis
- Relative blood volume monitoring (“Critline”)
- Biomarkers: ANP, BNP, NT-ProBNP levels

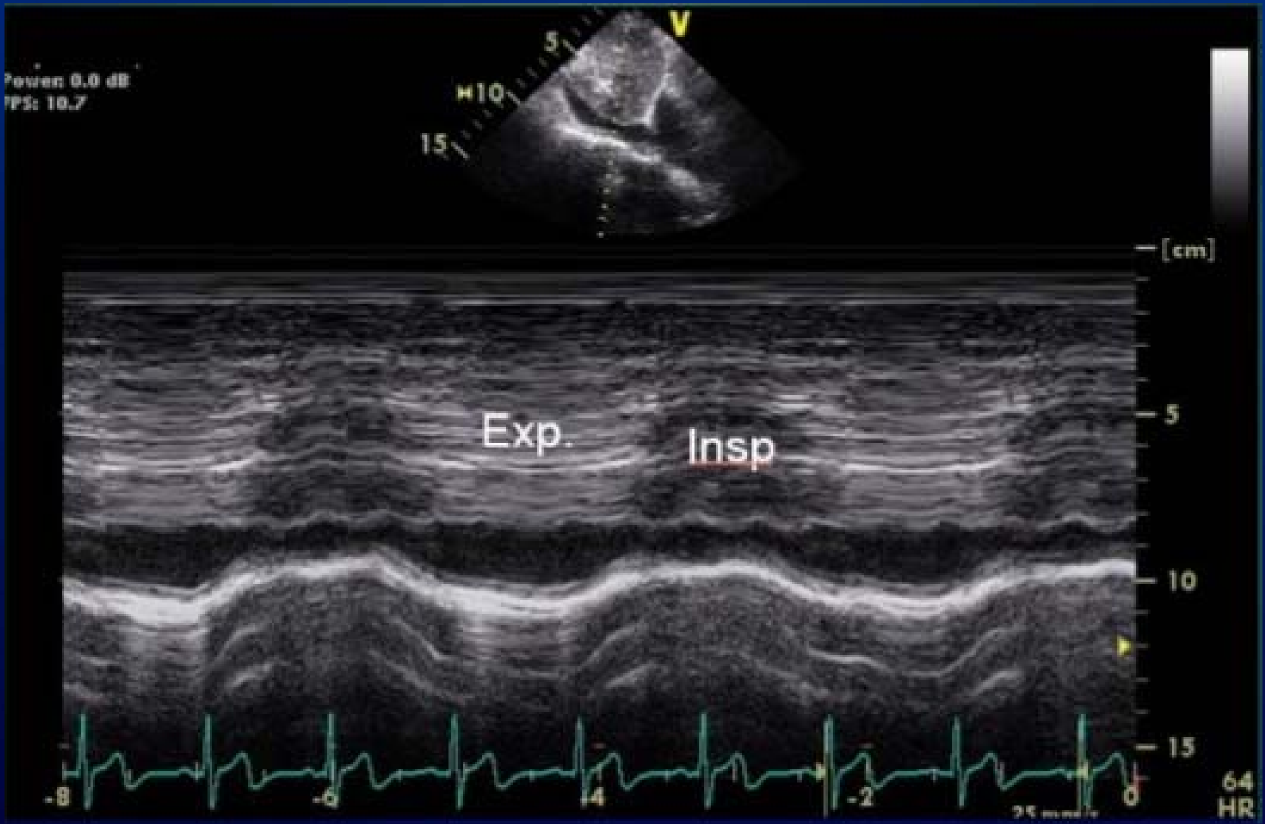
# US Lungs



“Comet-tail images” = reverberations created by reflection of US beam between pleura and thickened edematous interlobular septa

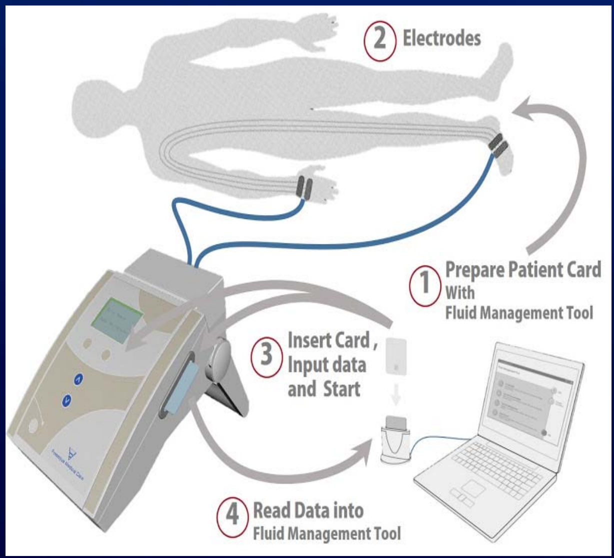
# US IVC diameter


Subcostal Longitudinal view



# Bioimpedance Analysis

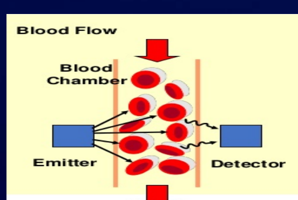
- Bioimpedance measures the resistance of body to applied alternating current flow.
- At low frequency current can only pass through ECF and at higher frequency, current can pass through ECF and ICF

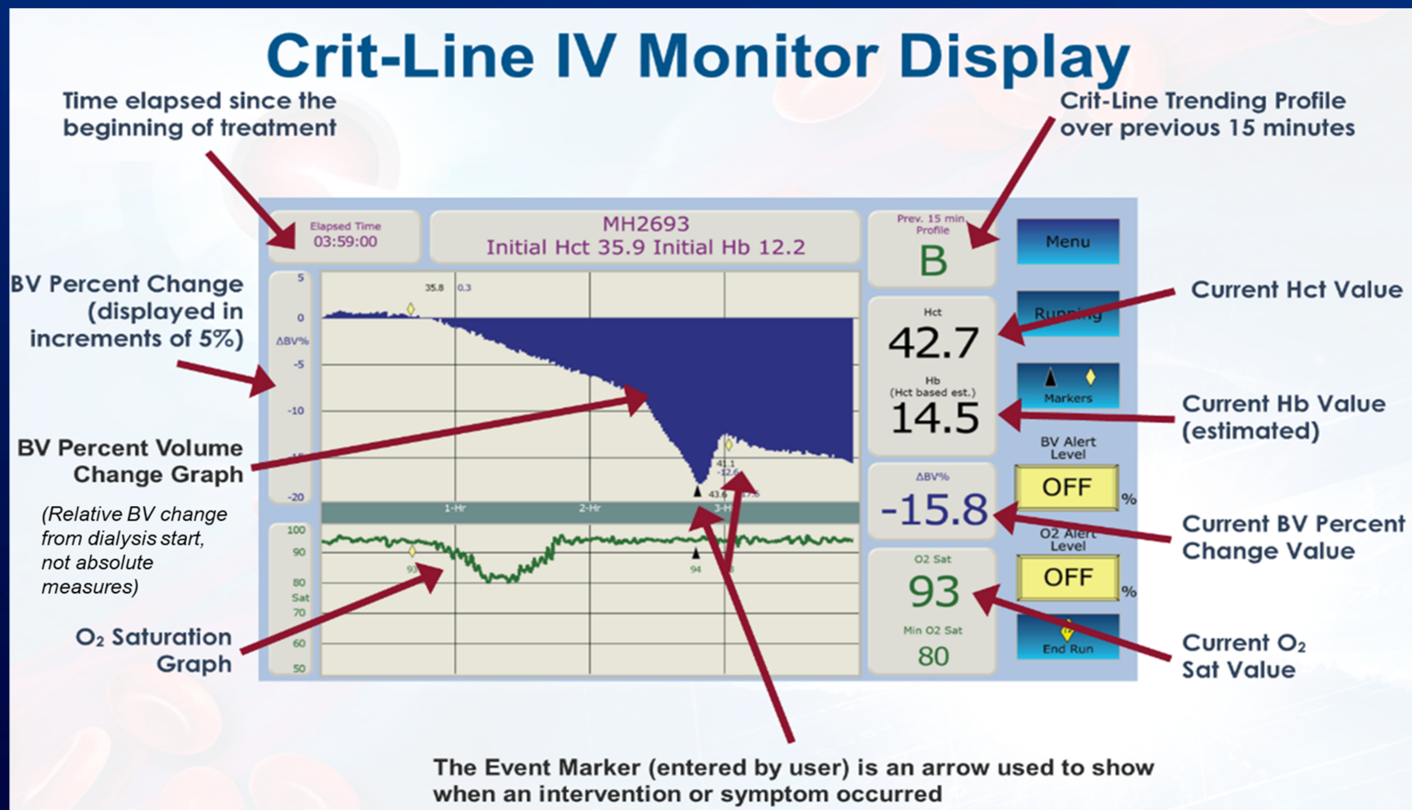




http://www.fmcna-crit-line.com/

# CRIT-Line: Optimize Fluid removal & effectively reach prescribed DW

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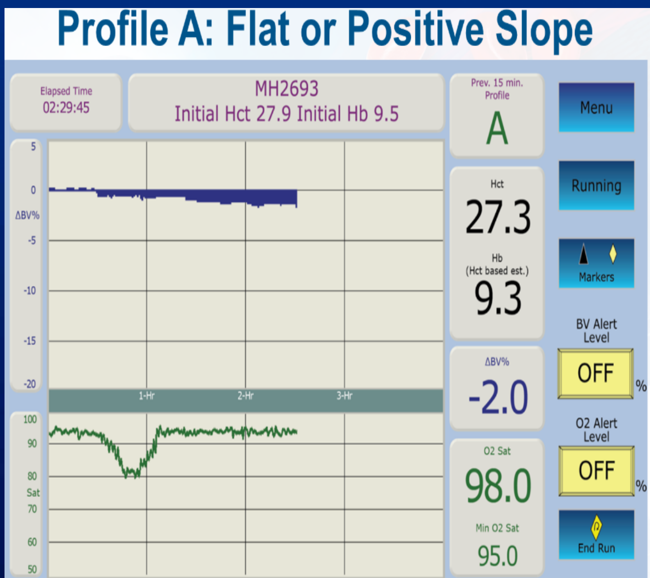
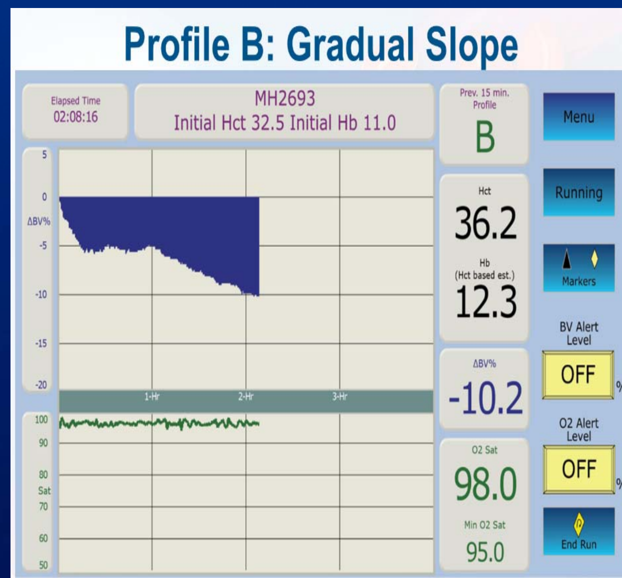
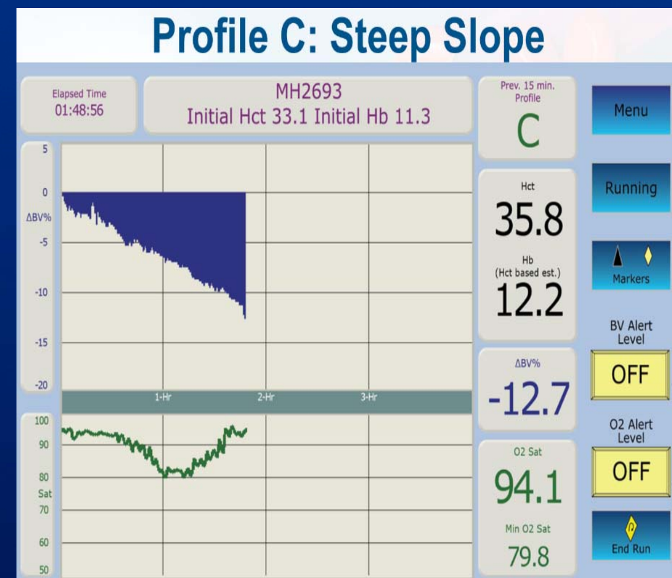



Plasma refill rate ≥ UFR
ΔBV% ≤ -3%/h
UFR may be increased without immediate risk of intradialytic symptoms

Plasma refill rate > UFR, best compromise
ΔBV% > -3%/h to ≤ 6.5%/h
Caution if approaching -6.5%

Plasma refill rate > UFR
ΔBV% > -6.5%/h
Higher risk for intradialytic symptoms
High risk: ΔBV > -8%/h or total change in BV > -16% at the end of 4 h dialysis session

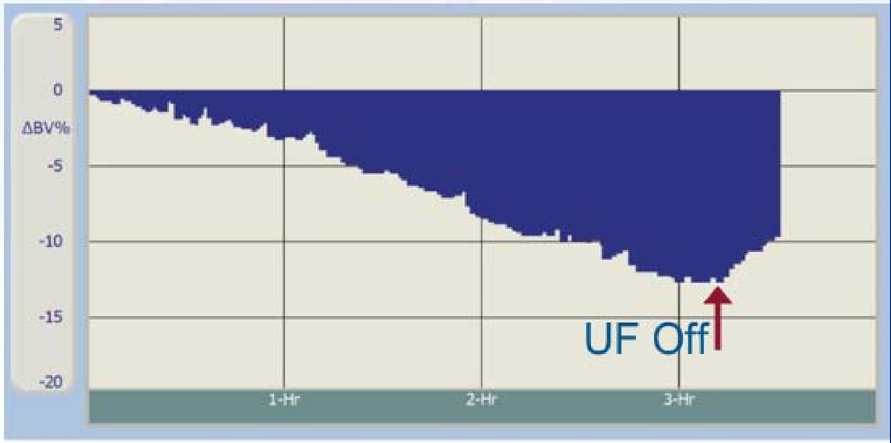
http://www.fmcna-crit-line.com/

Calculation
Current ΔBV = -10.2/2.13h = -4.79%/h

# Assessment of Plasma Refill

- Refill indicates fluid is shifting from the tissues to the vascular compartment
  - Additional fluid may be available for removal, if indicated

Refill indicated by Hct change ≥ 0.5/10min




- No refill indicates that fluid is not shifting to the vascular compartment
  - Additional fluid removal without increased risk of intradialytic symptoms is limited

# UFR or FRR: How much is safe?

Avoiding myocardial stunning and cardiac injury

Longer Td and slower UFR in HD: associated with reduced mortality in the DOPPS I & II combined (1997 – 2004): 22,000 HD patients, *R Saran et al. KI 2006; 69: 1222 – 1228.*

UFR > 10 ml/postHD wt/h associated with higher odds of IDH (OR 1.30, $p = 0.045$) and higher risk of mortality (RR 1.09, $p = 0.02$)

Association between high UFR and mortality in uremic patients on regular HD – A 5 y prospective observational multicenter study. *Movilli et al. NDT 2007; 22 (12): 3547 – 3552.* 287 prevalent HD patients (2000 – 2005).

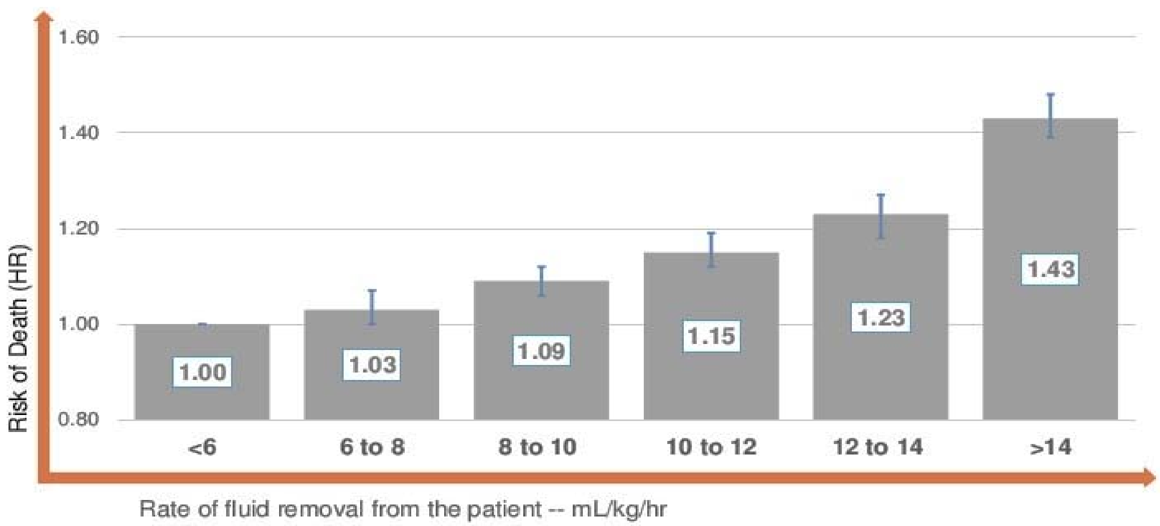
Mean UFR 12.7 ± 3.5 ml/kg/h. Multivariate Cox regression analysis showed a HR of 1.22, $p < 0.0001$ for mortality and UFR.

# Hazard ratios for different Ultrafiltration rates

## Ultrafiltration Rates over 6mL/kg/hr. Associated with Increased Risk of Death

AdvancingDialysis

### AGGRESSIVE FLUID REMOVAL RATES AND ALL-CAUSE MORTALITY




**METHODS:**

118,394 hemodialysis patients in DaVita facilities, 2008-2012, with mean follow-up of 2.3 years. Mean UF rate was characterized during a 30-day baseline interval.[1]

Fine and Gray proportional sub-distribution hazards regression models with kidney transplantation and dialysis modality change treated as competing risks were used to estimate the ultrafiltration rate and all-cause mortality association.[1]

[1]Assimon, M.M. et al. Ultrafiltration Rate and Mortality in Maintenance Hemodialysis Patients. Am J Kidney Dis. 2016;68(6):911-922

AdvancingDialysis.org

UFR ≤ 13 vs > 13: HR 1.31, ≤ 10 v > 10: HR 1.22

# UFR is a "reporting" measure for 2019 to 2022 PY

- Crownweb should have each patient's Kt/V date, Pre and Post dialysis weight for the three dialysis session during that week and number of dialysis sessions in the month.
- CMS Technical Expert Panel (2010) had recommended reporting proportion of patients with UFR > 15 ml/kg/h
- Chief Medical Officers of 14 largest US Dialysis providers in 2013: consensus on optimizing ECF status, fluid removal should be gradual.
- Kidney Care Quality Alliance (endorsed by National Quality Forum) and CMS proposed in 2015: UFR ≥ 13 & session length < 240 min. This has not been incorporated as performance measure.

My personal view: Track UFR, < 6, 6- 8, 8-10, 10 – 13, ≥ 13. Target 10 but do not exceed 13.

## Implications of Implementing UFR Target

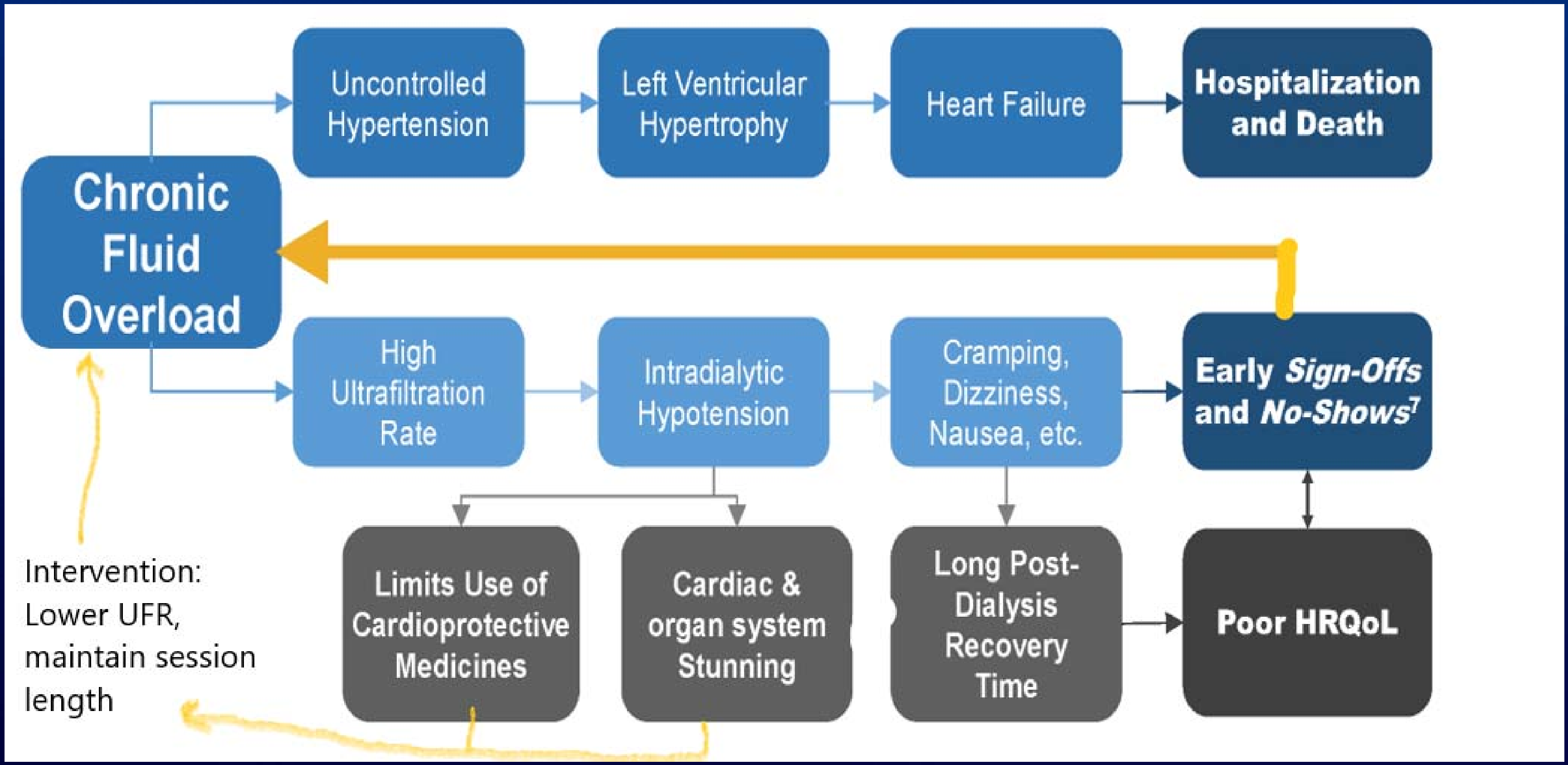
- Data from 152,196 HD patients from DaVita 2012 database.
- Examined target weight achievement pattern and quantified weight gains if UFR threshold was applied without treatment time extension or IDWG reduction.
- 27.1 ± 9.7% of patients had average post-HD weight ≥ 1 kg above or below the prescribed target weight.
- Without treatment time extension or IDWG reduction, implementation of UFR threshold (13 ml/kg/h) led to an average 1-month, fluid related weight gain of 1.4 ± 3 kg.

*Flythe et al. BMC Nephrology 2017; 18: 185*

## Implications of Implementing UFR Target

- Patients:
  - Limit sodium intake & IDWG
  - Be flexible to increase Td if needed
- Dialysis Prescription adjustment
  - Serum to Dialysate Na gradient
  - Decreasing dialysate temp
- Extension of dialysis time or frequency (Limiting factors: # shifts, staff availability)
- Increased cost

# Challenges with three-weekly HD



# Recommendations for Fluid Management on Dialysis

- Strict low sodium diet (dietitian consult) 2g /day
- Judicious use of diuretics in appropriate patients with residual kidney function
- Avoid intradialytic hypotension and symptoms
  - Hold BP meds if needed
  - Lower dialysate temperature
  - Serum – dialysate sodium differential
  - FRR < 10 ml/kg/h
- Target for weekly fluid removal & try to reduce post dialysis weight by 0.2 kg lower than previous session's post weight until target weight is reached
- Increase dialysis time and/or frequency
- Home Dialysis

## Proposed Metrics to assess adequacy of fluid removal

- BP control
- FRR
- Target weight achievement

## ESRD patient In-center HD
## 3.5 h x 3/week , Prescribed DW: 90 kg, D. Na: 140 mEq/L, Dialysate temp $37^0$C

| | |
|---|---|
| Monday<br>PreHD wt: 95 kg<br>Prev postHD wt 92, IDWG 3 kg<br>BP 150/100<br>1+ leg edema | RN assessment: Fluid overload;<br>Expected postHD wt will be 91.8 kg; UF needed to get to target weight = 3.2 L<br>UFR = 3200 ml/91.8 kg/3.5h = 10 ml/kg/h<br>Dial in on machine UF = 3500 ml, PostHD weight 91.8 kg |
| Wednesday<br>PreHD wt: 94 kg, IDWG 2.2 kg<br>BP 150/100<br>1+ edema | RN assessment: Fluid overload;<br>Expected postHD wt will be 91.6 kg, UF needed to get to target weight 91.6 = 2.4 L<br>UFR = (2400 ml/91.6kg)/3.5h = 7.5 ml/kg/h<br>Dial in on machine UF = 2700 ml, PostHD weight 91.6 kg |
| Friday<br>PreHD wt: 94 kg, IDWG 2.4 kg<br>BP 150/100<br>1+ edema | RN assessment: Fluid overload; UF needed to get to target weight of 91.4= 2.6L<br>Expected postHD wt will be 91.4 kg<br>UFR = (2600 ml/91.4kg)/3.5h = 8.1 ml/kg/h<br>Dial in on machine UF = 2900 ml, PostHD weight 91.4 kg |

# Conclusions

- Fluid overload is common and dangerous in ESRD with adverse short term and long term outcomes especially LVH and increased cardiovascular mortality
- Attention to adequacy of fluid management is needed
- Adjust dialysis prescription especially dialysate temp, dialysate Na, Td and/or frequency to target UFR < 10 to 13 ml/kg/h
- Tools available to guide UFR: Bioimpedence, Relative BV monitoring

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# Questions