Strategies to assess and manage hypervolemia—The invisible threat in dialysis

Rajiv Agarwal MD
Professor of Medicine,
Indiana University School of Medicine
Volume excess is common and costly.

- Admission for CHF in dialysis: 22% per year
- Volume overload needing acute dialysis: 14% per year
- Cost to Medicare (over 2.5 years): $266 million
The challenge of assessing volume—diagnosing hypervolemia
Seven methods to assess volemia

- History and examination
- Direct measurement of total body water
- Natriuretic peptides
- Bioimpedance analysis
- Relative plasma volume monitoring
- Blood pressure monitoring
- Echocardiogram
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Pedal edema is not a volume marker

- Pedal edema is not associated with:
  - IVC diameter
  - BNP
  - Relative plasma volume
  - Inflammation markers

Pedal edema associates with obesity, age, and LVH

Odds ratio of Pedal Edema in HD

- BMI <25 kg/m2 (Normal or Underweight)
- BMI 25 to 29.9 kg/m2 (Overweight)
- BMI >30 kg/m2 (Obese)

LV mass < median (68.8 g/m2.7) LV mass ≥ median (68.8 g/m2.7)

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TECHNICAL NOTE

Measuring total body water in peritoneal dialysis patients using an ethanol dilution technique

NAOMI V. DAHL, EDWARD F. FOOTE, TOROS KAPOIAN, CAROLINE A. STEWARD, and RICHARD A. SHERMAN

University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, New Brunswick, and College of Pharmacy, Rutgers, The State University of New Jersey, Piscataway, New Jersey, USA
Volume of distribution of alcohol = TBW
Drawbacks

- Several hours for measurement
- Alcohol exposure
- No data on how to use this information
Technical Note

A non-invasive, on-line deuterium dilution technique for the measurement of total body water in haemodialysis patients

Cian Chan¹, David Smith², Patrik Spanel³, Christopher W. McIntyre⁴ and Simon J. Davies¹,²
A non-invasive, on-line deuterium dilution technique for the measurement of TBW in haemodialysis patients

Fig. 1. The subject exhales gently into a disposable tube; breath is sampled from a calibrated capillary into the flow tube where it mixes with protonated water (H₂O⁺) created by a microwave discharge. Whilst flowing down the tube, driven by a constant stream of the inert gas (e.g. helium), breath water vapour forms clusters with the H₂O⁺, and those with an m/z ratio of 74 will contain deuterium. A relative increase in these water clusters, when compared to m/z 75 detected by the mass spectrometer, enables calculation of deuterium enrichment.
Fig. 4. Deuterium kinetics: (A) average equilibration curve of breath D following oral ingestion; the initial large peak is due to D still present in the mouth. Subsequently there is gastrointestinal absorption and then equilibration by 2 h. (B) Over the next few days there is exponential clearance of D from the breath (mean values, those marked PRE are pre-dialysis), predominantly during dialysis treatments (shown as vertical arrows) such that it is cleared by 10 days.
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B-type natriuretic peptide is not a volume marker among patients on hemodialysis

Rajiv Agarwal

Correspondence and offprint requests to: Rajiv Agarwal; Email: ragarwal@iupui.edu

Indiana University School of Medicine and Richard L. Roudebush Veterans Administration Medical Center, Indianapolis, IN, USA

Keywords: BNP, dry weight, ESRD, hemodialysis, hypertension
In the DRIP trial, BNP did not...

- Decline more with ultrafiltration
- Associate with more weight loss
- Associate with a greater improvement in interdialytic ambulatory BP
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Whole body BIA can detect changes in ECW

Fisch BJ et al., Kidney Int 49: 1105, 1996
Segmental resistance increases with UF-dialysis

Zhu F et al, ASAIO Journal 44: M541, 1998
Does BIA-guided dry-weight management result in better BP, TOD, outcomes?

- No study so far
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Blood Volume Monitoring

Disposable Blood Chamber

Sensor Clip
Disposable Blood Chamber
Sensor Clip
Liquid Crystal Display
RPV Principle

Euvolemic Interstitial Space → Vascular Refill → Increasing Hemoc-Concentration → Vascular Space → Ultrafiltration
RPV Principle

Hypervolemic Interstitial Space

Vascular Refill

No Hemo-Concentration

Vascular Space

Ultrafiltration
RPV Tracing

Time on Dialysis (hrs)

Relative Plasma Volume (%)

80
85
90
95
100
105
RPV and Volemia

- Pre-specified secondary analysis of 150 HD patients in DRIP Trial
DRIP Trial

- 150 patients
  - On dialysis ≥ 3 months
  - Ambulatory BP ≥ 135/85

- 100 patients ultrafiltration group
  - Randomized
  - 8 weeks
  - Ambulatory BP

- 50 patients control group
  - 8 weeks
  - RPVM
  - ABP

Study overview

◆ Design: Diagnostic test study
◆ Test: RPV monitoring
◆ Comparison standards of volume state:
  ◆ 1. Change in RPV slope
  ◆ 2. Ambulatory BP change
Control Corrected Change in Ambulatory BP in Ultrafiltration Group

Change in Ambulatory BP (mmHg)

-14 -12 -10 -8 -6 -4 -2 0 +2

P < 0.05

1 (steepest)

2 Quartile of RPV Slope

3

4 (flattest)

0 1

-3.2

-11.1

-12.6

Ultrafiltration volume not predictive of mortality

Number at risk
Higher UF Volume 151 133 120 99 82 70 52 42 39 36 23 14
Lower UF Volume 142 125 109 100 88 69 54 47 45 38 25 18

Logrank p = 0.208

Agarwal R, Hypertension 56: 512, 2010
But flatter RPV slopes associated with a higher mortality

Logrank $p = 0.011$

Agarwal R, Hypertension 56: 512, 2010
Relative plasma volume is independently associated with mortality

Hazard Ratio for death

- Adjusted (age, sex, race, CVD, BP meds, dialysis vintage, albumin, Hgb)
- Adjusted + UF volume
- Adj + UFR
- Adj + UFR/kg
- Adj + UFR/kg + ABPM

$p=0.02$  
$p=0.008$  
$p=0.002$  
$p=0.001$  
$P<0.001$

Agarwal R, Hypertension 56: 512, 2010
Does RPV-guided dry-weight management result in better BP, TOD, or outcomes?
RPV Monitoring Randomized Clinical Trial

- Crit-Line Intradialytic Monitoring Benefit (CLIMB) Study
- Multicenter trial with 6 centers in the U.S. and Canada

CLIMB Study

443 patients
On dialysis ≥ 2 months

2 weeks

RPV monitoring

227 patients RPVM group
Randomized

216 patients control group

6 months

CLIMB Results

- RR for non-access related admit in RPVM group 1.49
  - (P = 0.017)

- Mortality 8.7% in RPVM group vs. 3.3% for control
  - (P = 0.021)

However…

“Algorithm use was encouraged, but not mandated…”

“Highly variable implementation of the monitoring and interventional algorithm occurred within and across dialysis units.”
Control Group RPV Slope Baseline Distribution

- Steep: 8%
- Flat: 32%
- Intermediate: 60%

Control Group RPV Slope Final Distribution

- Steep: 11%
- Intermediate: 23%
- Flat: 65%

Control group has fewer patients with flat slopes despite no intervention!

Does RPV-guided dry-weight management result in better BP, TOD, or outcomes?

Don’t know, we need a better study!
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Systolic Home BP of $\geq 150$ mm Hg has a sensitivity of 80% and specificity of 84% in diagnosing interdialytic ambulatory hypertension.

Is out of dialysis unit BP of prognostic value?

- Baseline cohort followed for 2 years for all-cause mortality.
- 46 patients (31%) died.
- Quartiles of systolic BP associated with mortality in a Cox model.
Out of dialysis unit BP are of greater prognostic significance.

"Best home BP" 125-145 mm Hg

Best ABP 115-125 mm Hg

P = 0.05

Hazard Ratio of All Cause Mortality

Does Home BP-guided BP management result in better BP, TOD, outcomes?
Home BP in HD—Trial Design

Home BP Group (n=34)
- Adjust antihypertensive medications
- 24-hr Ambulatory Blood Pressure + Echocardiogram

Dialysis Unit Group (n=31)
- Adjust antihypertensive medications
- 0 • ABPM
  • Echocard
- 6 months • ABPM
  • Echocard

RCT shows that ambulatory BP improves with the use of home BP monitoring

No change seen on echo LVH

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IVC Diameter – End Expiration

1.89 cm = 10.5 mm/m²
IVC Diameter – End Inspiration

1.83 cm
CI = 3.1%
Conclusions The inferior vena cava and left atrial diameters are echocardiographic parameters that are responsive to probing dry weight; thus, they reflect excess volume. However, echocardiographic volume parameters are poor determinants of interdialytic BP, and their change does not predict the BP response to probing dry weight.

Pulmonary Congestion Predicts Cardiac Events and Mortality in ESRD

Carmine Zoccali,* Claudia Torino,* Rocco Tripepi,* Giovanni Tripepi,* Graziella D’Arrigo,* Maurizio Postorino,* Luna Gargani,† Rosa Sicari,† Eugenio Picano,† and Francesca Mallamaci,* on behalf of the Lung US in CKD Working Group

*National Research Council-Institute of Biomedicine, Clinical Epidemiology and Physiopathology of Renal Diseases and Hypertension, Reggio Calabria, Italy; and †National Research Council-Institute of Clinical Physiology, Pisa, Italy

Lung comets

Jambrik Z et al. Am J Cardiol 93: 1265, 2004
Lung comets—marker of pulmonary congestion correlated with ACM + cardiac events

Figure 1. Kaplan–Meier survival analyses of all-cause mortality and fatal and nonfatal cardiac events according to the BL-US.
What can you do today? ...

- Be aware of occult hypervolemia.
- Ask yourself the question: could these symptoms be due to hypervolemia?
  - If discharged from the hospital, probe dry weight.
  - If BP runs low and the patient is repeatedly hospitalized due to “pneumonia”, probe dry weight
  - If home BP is high, probe dry weight
  - Technology is unreliable, but RPV is the tool I use as my eyes to volume.
- Prescribe at least 4 hours of dialysis.
- If they cut their time or miss dialysis, they are likely not euvoletic.
  - Root cause analysis: transportation, child-care, cramps etc
  - Engage the dietitian, social worker, spouse, the patient to dialyze adequately.
Take home message...

- Dialysis is not just about Kt/V, Hgb, Phos….
- Volume is important.
- We CAN do better!