Management of Intravascular Volume in the ESRD Patient: Focus on Bioimpedance and Ultrasound

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Conflicts of Interest

- None

A Measure of Fluid Removal Adequacy

- Despite advances in assessment of solute removal adequacy, we still are in the relative "dark ages" in terms of assessing a given patient's volume status and their needs for fluid removal.
- Current methods are largely "trial and error" in nature and attempt to define a "dry weight" for dialysis patients based upon the lowest weight a patient can tolerate without the development of symptoms or hypotension
- The degree of imprecision is great as noted by the high rate of intra-dialytic symptoms as well as chronic volume overload and poor BP control
- Poor outcomes of ESRD patients have been related to our inability to properly guide volume management

Jaeger JQ, Mehta RL. J Am Soc Nephrol 1999; 10: 392-403

"You've been such a good patient, you may help yourself to a leech, child."

Volume Overload in Dialysis Patients

Volume Overload

Inadequate Removal
- Left ventricular hypertrophy
- Hypertension
- Congestive heart failure
- Arrhythmias
- Sudden cardiac death
- Dyspnea, poor quality of life

Excessive Removal
- Intradialytic hypotension
- Myocardial stunning → fibrosis
- Acute/subacute stroke → dementia
- Access thrombosis
- Bowel ischemia → endotoxemia
- Loss of residual kidney function
- Cramping, postdialysis fatigue → poor QOL

Morbidity and Mortality

Laupacis A, et al Nephron 1992; 60: 302-306
Fishbane S et al. Am J Kidney Dis 1996; 28: 257-261

Some "Simple" Concepts

- Fluid overload refers to an excess of extracellular volume
- Fluid depletion refers to a deficit in extracellular volume
- Hypovolemia is the reduction of blood volume which is typically associated with symptoms such as tachycardia and hypotension depending upon its severity
- "Dry weight" has many definitions:
  - defined as the post-dialysis weight at which blood pressure remains normal during the interdialytic period without use of antihypertensives despite weight increase.
  - reflects the lowest weight a patient can tolerate without intradialytic symptoms and hypotension in the absence of overt fluid overload
  - amount of body mass (weight) without extra fluid (water)
  - normal weight without any extra fluid in your body

www.aakp.org; www.kidney.org; Kidney Int Suppl (2011). 2013 Dec; 3(4): 377–379.; J Am Soc Nephrol 1999, 10: 392-403

Problems with current concept of dry weight

- Assumes that BP and extravascular volume have a direct correlation which is not always true:
  - Three studies: BP did not differ between patients with or without signs of volume overload or the association between BP and volume status was variable
  - Wabel et al: 13% of patients are hypertensive with no evidence of volume overload and 10% of patients were normotensive despite large excesses in extracellular volume (by bioimpedance)

Wabel P et al Nephrol Dial Transplant 2008; 23: 2965-2971
Dionisio P, et al. Blood Purif 1997; 15: 25-33

Ascertaining Dry Weight

- Important to realize that intradialytic hypotension is a common consequence of these “dry weight challenges” as ultrafiltration rates may be excessive for some patients to reach these goals.
- In these cases, hypotension should not be confused with attaining (or being below) dry weight.
- Thus, the over reliance on blood pressure as the marker for volume status is problematic and other methods of dry weight assessment are needed
- Perhaps, a static concept such as dry weight needs to be abandoned
- A better term may be normal hydration weight

What is the goal of current therapies?

- To attain a reproducible, accurate lower than physiological dry weight immediately post-dialysis (allows for weight gain in the inter-dialytic period)
- This would allow a time-averaged physiological dry weight throughout the interdialytic period
- Objective tools that are easily applied both during dialysis and throughout the inter-dialytic time period that determine optimal weight

Techniques to Assess Dry Weight

- Physical Examination
- "Experimental/empirical" probing
- Blood volume monitoring
- Bioimpedance
- Vena Cava Diameter
- Thoracic Ultrasound
- Natriuretic Peptides

Physical Examination

- Certainly, a key part of the assessment
- Dialysis units tend to be a poor place to do an accurate assessment
- Critical care literature is consistent that while the presence of jugular venous distension, rales and edema are consistent with volume overload, their absence does not exclude volume overload and the examination has poor sensitivity and specificity overall
- Not sensitive enough to help determine "dry weight?

McGee SR. Am Heart J 136:10–18, 1998

Probing Dry Weight: Empirical

- Addition weight loss/ultrafiltration is prescribed without changing the time or frequency of sessions
- If ultrafiltration is not tolerated due to muscle cramps, need for excessive saline, or symptomatic hypotension, the additional prescribed weight loss can be reduced by 50%.
- If ultrafiltration was still not tolerated, the additional weight loss can be further reduced by 50% until even 0.2-kg incremental weight loss per dialysis was not tolerated. At this point, the patient was said to be at his or her dry weight.
- However, numerous confounders make this technique less than ideal

Bioimpedance

- Effective resistance (inversely proportional to TBW) and reactance of biological tissue (proportional to cell mass) to alternating current
- Relies on passing a low-strength AC through the body
  - Multi-frequency devices predominant
    - Whole body bioimpedance spectroscopy (BIS)
    - Segmental bioimpedance spectroscopy (BIS)
      - Segmental BIS methods take readings in various segments of the body (arms, legs, calves, and trunk) and are generally continuous over the period of measurement
  - Monofrequency devices of questionable value in dialysis patients

Dou Y, et al. Semin Dial 2012; 25: 377-387

Bioimpedance Guidance of Fluid Management

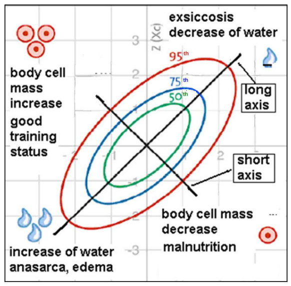
- I. Continuously sample changes in bioimpedance during UF so that as the rate of change in bioimpedance with fluid removal levels off, the patient should be approaching dry weight.
- II. Use bioimpedance to determine a normally hydrated weight that would be the goal of therapies and dietary interventions.
- III. Measure serial changes in pre- and post-dialysis bioimpedance to assess fluid status and body composition

Bioimpedance Vector Analysis (BIVA)

- Pioneered by Piccoli
- The bioimpedance (resistance-reactance) vector length reflects the degree of tissue hydration, and the vector lengthens with ultrafiltration (lower body hydration).
- Shorter predialysis bioimpedance vectors, indicating greater soft tissue hydration, are associated with diminished survival in hemodialysis patients, consistent with the clinical observations linking longevity to maintenance of dry body weight
- Vector analysis based upon normal population and not dialysis patients
- May not be able to quantitate fluid status in individual patient

BIVA: Results

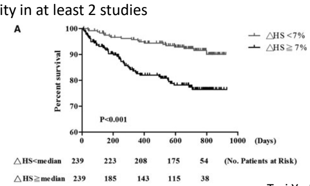
Allows determination of body water and cell mass (nutritional status)



From: Walter-Kroker et al. Nutrition Journal 2011 10:35 doi:10.1186/1475-2891-10-3

Whole Body Bioimpedance Spectroscopy

- Uses alternate current frequencies and mathematical modeling for estimation of fluid volumes of extracellular and intracellular compartments
- Derives fluid status relative to a healthy population
- Has been correlated with excessive cardiovascular mortality and morbidity in at least 2 studies



Tsai Y et al. CJASN 2015; 10:39

Regional Bioimpedance Spectroscopy

- Alternative to whole body readings
- Can be done in one limb
- Practically challenging as need to keep limb (calf) in horizontal position and take measurements of limb circumference
- Validation data is scant as well.

Zhu F, et al. Blood Purif 2015; 39:25-31

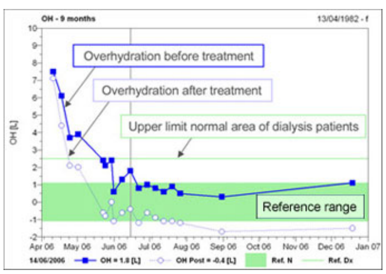
Body Composition Monitor (Fresenius®)

The body composition model describes the intra and extracellular water content of lean tissue mass, adipose tissue mass and excess fluid (overhydration).

Of note, volume management strategies using these devices have not been well studied

http://www.bcm-fresenius.com/21.htm

Body Composition Monitor®: Trends



http://www.bcm-fresenius.com/20.htm#Fluid Management Tool – Illustration of results

UK NICE Assessment of BCM

- "There is currently not enough evidence to recommend the routine adoption of the BCM – Body Composition Monitor to guide fluid management in people with chronic kidney disease having dialysis in the NHS. Further research is recommended to show the effect of using the BCM – Body Composition Monitor on clinical outcomes"

NICE National Institute for Health and Care Excellence

https://www.nice.org.uk/guidance/dg29/chapter/4-Evidence

Bioelectrical Impedance Analysis: Limits

- Measures body composition indirectly
- Accuracy largely depends on mathematical models and their assumptions which have been validated in select populations which are usually of European descent and do not have kidney disease
- Influenced by pacemakers

Bioimpedance: Overall Impressions

- Used effectively in research studies
- Clinically, not well studied in the determination of dry weight in patients
- Canadian Agency for Drugs and Technologies in Health:

"Five studies on the effectiveness of bioimpedance spectrometry devices were included in the review. The literature search did not identify any cost-effectiveness analyses or clinical guidelines. The included studies showed limited evidence that the use these devices as adjunctive tools in fluid-management might be associated with better patient outcomes such as decreased blood pressure, reduced fluid overload, and decreased left ventricular mass index."

- Lack trials based upon clinical endpoints demonstrating effectiveness
- Effectiveness largely measured by changes in fluid status

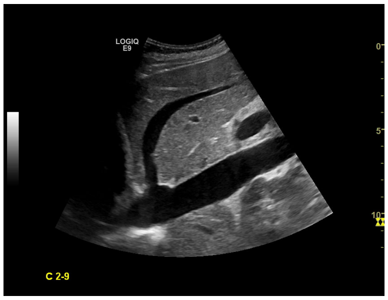
Canadian Agency for Drugs and Technologies in Health; 2014 Mar 17

Inferior Vena Cava Monitoring

- Most intravascular volume in venous system and changes in ECV parallel the changes in IVC diameter in most cases
- Diameter and collapsibility of IVC assessed by US
- Caveats:
  - Wide variation in IVC diameter in normals
  - Single measurements are not helpful
  - Significant, inverse correlation between IVC diameters and heart rate (ideally, corrected values to heart rate)
  - Not reliable with tricuspid valve disease
  - Significantly affected by increased intra-abdominal or intra-thoracic pressure
- Serial measurements allow changes in intravascular volume to be estimated
- Can be technically difficult
  - Experienced user
  - Difficult if patient not supine

Rosner, MH and Ronco C. Semin Dial 2014; 27: 538-541

IVC Ultrasound



http://www3.gehealthcare.com.au/en-au/products/categories/ultrasound/logiq/logiq_e9_-_xdclear

IVC Distensibility Index

- Difference between end-inspiration (Dmax) and end-expiration (Dmin) IVC diameter divided by Dmin.
- An index threshold of 18% in a study of 23 patients was found to have a 90% sensitivity and specificity to distinguish a response to volume expansion
- Has shown correlation with bioimpedance in one study
- Use in chronic HD unit presents significant challenges in determining hydration status and is influenced by diastolic dysfunction and right-sided heart failure

J Ultrasound 2015; 18: 343-348
Intensive Care Med 2004; 30: 1740-1746

Understanding the B-Line on Lung Ultrasonography

- Ultrasound beams meet interlobular septum that is thickened and creates a reverberation artifact resulting in a hyperechoic line perpendicular to the pleural surface= B line
- B lines:
  - Arise from the pleural surface
  - Move with pleural line
  - Well defined
  - Hyperechoic and spread out without fading
  - Reach the bottom of the screen
- They represent:
  - An alveolar or interstitial abnormality
  - Such as: cardiogenic pulmonary edema, accumulation of excess lung water, pneumonia, lymphangitic carcinoma, ARDS or pulmonary fibrosis

Ross DW et al. Clin Kidney J 2018; 11: 172-178

Chest B-Lines

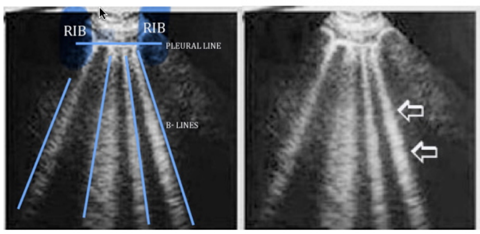


Figure C: B lines, Lichtenstein et al.

From: https://drhem.wordpress.com/tag/ultrasound/

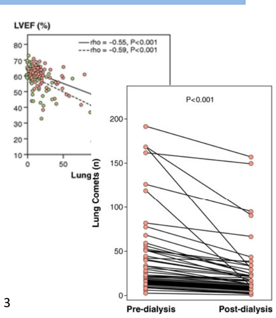
B-Lines

- Sonographic B-lines ('lung comets") have been shown to correlate with the presence of extravascular lung water.
  - Acoustic reverberations resulting from increased lung water and subpleural interstitial edema
  - Relate to chest radiography Kerley B-lines
- Characterization of the dynamics of B-lines, specifically their rate of disappearance as volume is removed, has been utilized to better assess dry weight in dialysis patients
- The number of B-lines is associated with the accumulated weight before treatment as well as with the residual weight after dialysis.
- Important to note that lung water content also depends upon
  - Left ventricular function (left ventricular end-diastolic pressure)
  - Lung permeability

Noble VE et al. Chest 2009; 1433-1439

B-Line Score in ESRD Patients

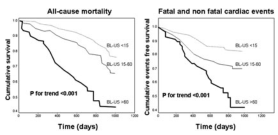
- High intra- and interobserver reproducibility
- High technical reproducibility
- Takes about 2-4 hours of training
- Score reflects the total number of comets measured at intercostal spaces locations bilaterally
- Numerous protocols ranging from 28 to 2 zone measurement or even qualitative assessment
- 3 categories of increasingly severe pulmonary congestion (mild: 14 comets; moderate: 14 to 30 comets; severe: > 30 comets)
- Early studies showed:



Mallamaci F et al. JACC 2010; 3

Lung Ultrasound and Volume Management

- Patients with very severe congestion (defined by the number of lung comets)had a 4.2-fold risk of death and a 3.2-fold risk of cardiac events compared to those patients having mild or no congestion.
- B-lines are reduced after dialysis, generally in proportion to the amount of fluid removed
- Studies are small, generally underpowered and use various “gold standards”.
- Few studies link decision making based upon B-line scores with outcomes



Zoccall C, et al. J Am Soc Nephrol 2013; 24: 639-646
Vituri N et al. Int Urol Nephrol 2014; 46: 169-174

Hidden Lung Congestion in ESRD Patients

- Study of 88 PD patients revealed mild to severe pulmonary congestion in 46% of patients using lung US in the absence of signs and symptoms of fluid overload
- In 270 HD patients, lung US revealed moderate-to-severe pulmonary congestion in 58% of which 38% were asymptomatic.
- Lung US findings have correlated with decreased physical activity in both PD and HD patients
- However, correlation with other methods on volume assessment is moderate to poor.

Di Nicolo P et al. Blood Purif 2017; 44:1-7

Lung US in ESRD Patients

- Useful tool for monitoring congestion reduction in response to dialysis treatment and ultrafiltration amounts
- Guides needs for additional fluid removal
- Correlates with interdialytic weight changes and UF volumes
  - Removal of 500 ml of ultrafiltration was shown to correlate in an average decrease of 2.7 B lines
- More sensitive than physical examination
- Correlates with LV function on echocardiography
- Correlates with changes in IVC diameter
- Positive relationship with natriuretic peptide levels
- Conflicting results correlating to BIA
- May correlate with improvements in physical activity

Noble VE, et al. Chest 2009; 135: 1433
Trezzi M et al. Intern Emerg Med 2013; 8: 409

Comparison of B-Line Scores with Other Methodologies

- Recent study in 53 chronic HD patients
- Compared volume assessment (hydration status) between IVCD, BLS, BIA, Crit-line
- Used IVCD as standard

Status	Method	AUC	Sensitivity	Specificity
Overhydration	BLS	0.81	77	74
	BIA	0.71	90	45
	Crit-line	0.61	82	39
Underhydration	BLS	0.83	78	73
	BIA	0.76	71	80
	Crit-line	0.53	68	47

Alexiadis G, et al. Int Urol Nephrol 2017; 49: 525-532

Summary

- Assessment of baseline volume status in ESRD patients is difficult and there is no easy to use gold standard to determine the amount of ECF volume expansion
- Various tools are available to aid clinicians to determine if a patient remains volume expanded after ultrafiltration. However, all require serial measurements and have their caveats
- Critical is that patient-centered, serial measure be used and that the center has technical expertise.
- Information from any one source of volume assessment needs to be integrated with data from the physical examination, serial weights, response to ultrafiltration and symptoms

Conclusions

- We need a measure of volume adequacy
- No current methods are ideal
- Careful, serial assessment of patients is critical and ideally should include a variety of methodologies including:
  - Physical examination and monitoring weight
  - Blood volume monitoring
  - Bioimpedance
  - Chest Ultrasound/IVC Ultrasound
  - Natriuretic peptide levels
- Practical trials on device-guided therapies that trigger clinical decisions are needed