Assessment Of Fluid Status in PD

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EPIDEMIOLOGY OF FLUID STATUS IN PD

- Fluid overload(FO), common in PD patients, is linked directly to increased cardiovascular(CV) morbidity and mortality
- Congestive heart failure, is associated closely with fluid overload which accounts for approximately 5% of all-cause mortality in prevalent dialysis patients
- Volume control is a modifiable risk factor

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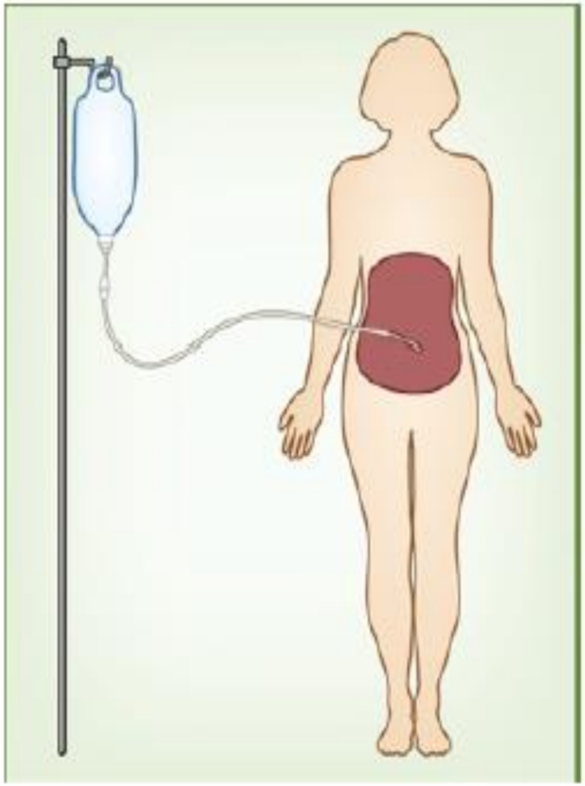
Physical condition

Co-morbidity
Cardio-pulmonary function
Inflammation
Nutritional status
Frailty

Residual renal function

Use of angiotensin converting enzyme inhibitors/angiotensin receptor blockers
Use of diuretics
Exposure to nephrotoxic agents
Exposure to hemodialysis
Episodes of dehydration
Peritonitis episodes
Episodes of intercurrent illness
Use of biocompatible dialysate
Dialysis vintage



Patient related factors

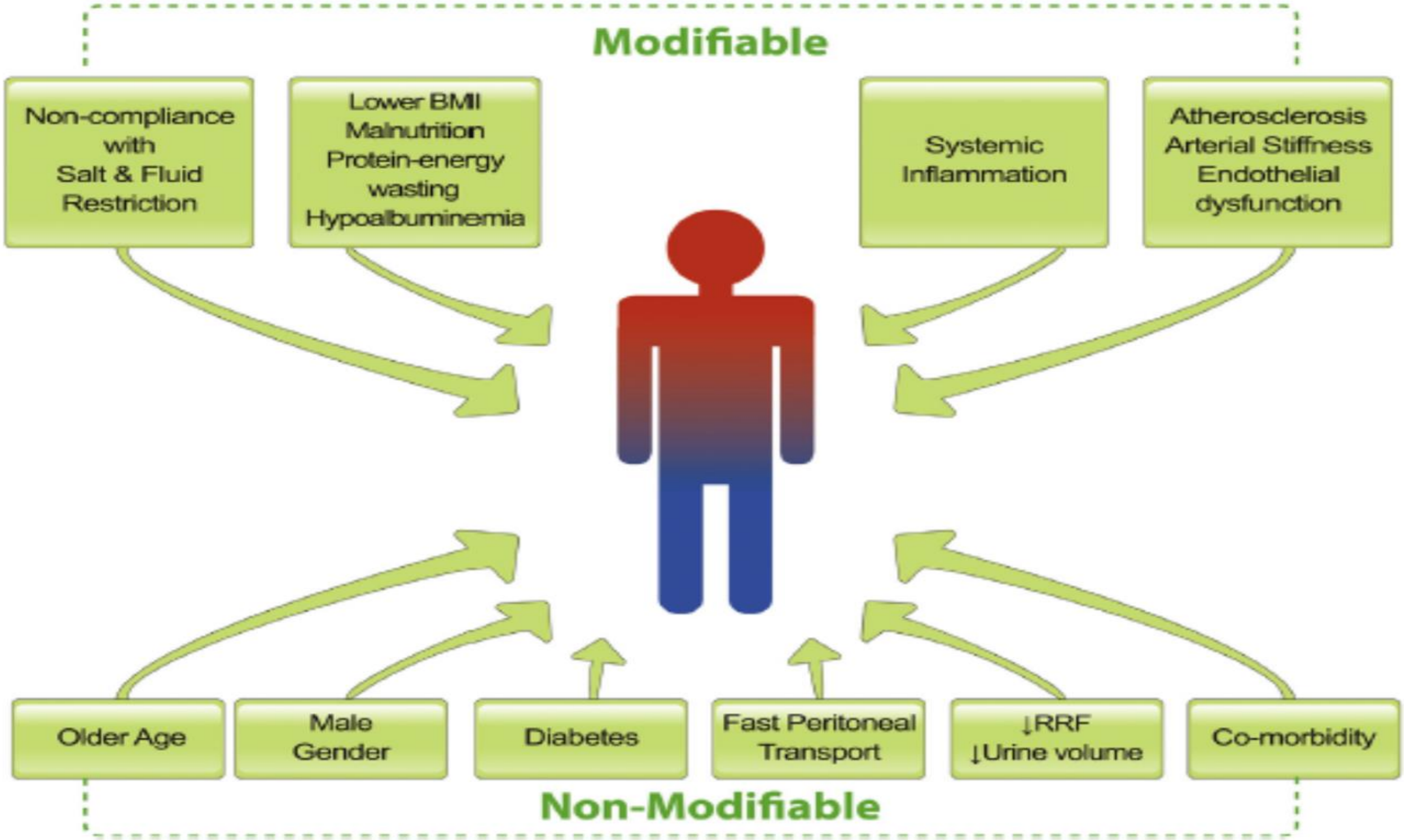
Level of training and health literacy
Social support and interaction with nursing team
Mood
Adherence to salt and water restriction
Tolerance of peritoneal dialysis prescription
Blood glucose control
Self monitoring of blood pressure and weight

Dialysis related factors

Mechanical factors eg catheter function, leaks, herniae
Membrane function & transport status
Peritoneal dialysis prescription to enhance ultrafiltration
– automated peritoneal dialysis, glucose exposure, use of icodextrin
Sodium losses
Protein losses

Factors affecting the volume status of a patient on peritoneal dialysis

Modifiable and nonmodifiable factors influencing fluid status



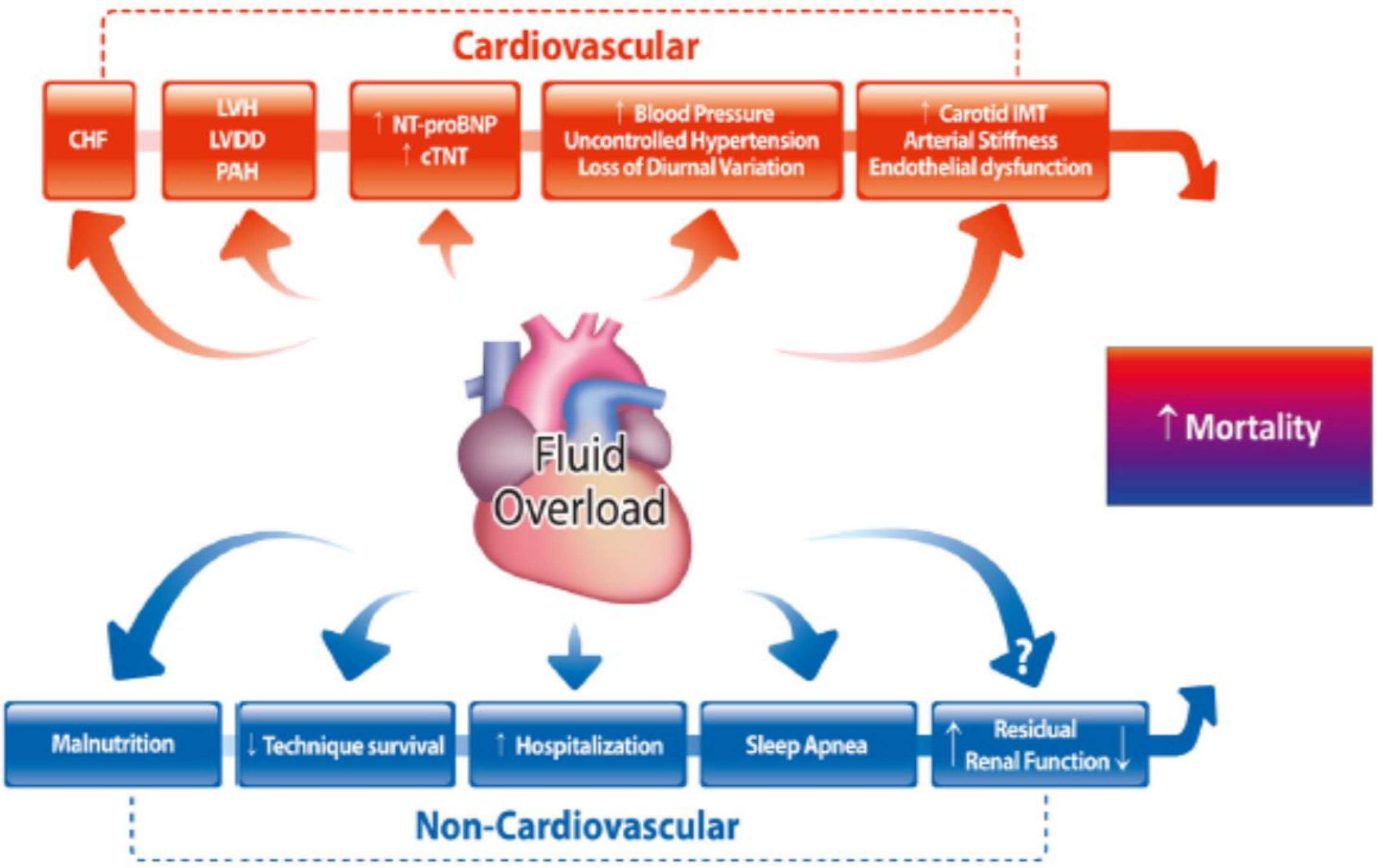
Evolution Over Time of Volume Status and PD-Related Practice Patterns in an Incident Peritoneal Dialysis Cohort

Wim Van Biesen,[1] Christian Verger,[2] James Heaf,[3] François Vrtovsnik,[4] Zita M. Leme Britto,[5] Jun-Young Do,[6] Mario Prieto-Velasco,[7] Juan Pérez Martínez,[8] Carlo Crepaldi,[9] Tatiana De los Ríos,[10] Adelheid Gauly,[10] Katharina Ihle,[10] and Claudio Ronco,[9] for the IPOD-PD Study Group

- The initiative for patient outcomes in dialysis - peritoneal dialysis (IPOD- PD) study of 1,092 patients from 135 centers in 32 countries investigated the baseline hydration status in Incident PD patients, finding that the majority(56.4%) of patients was overhydrated already before the start of PD

CJASN 14: 882–893, June, 2019

Consequences of fluid overload in PD patients



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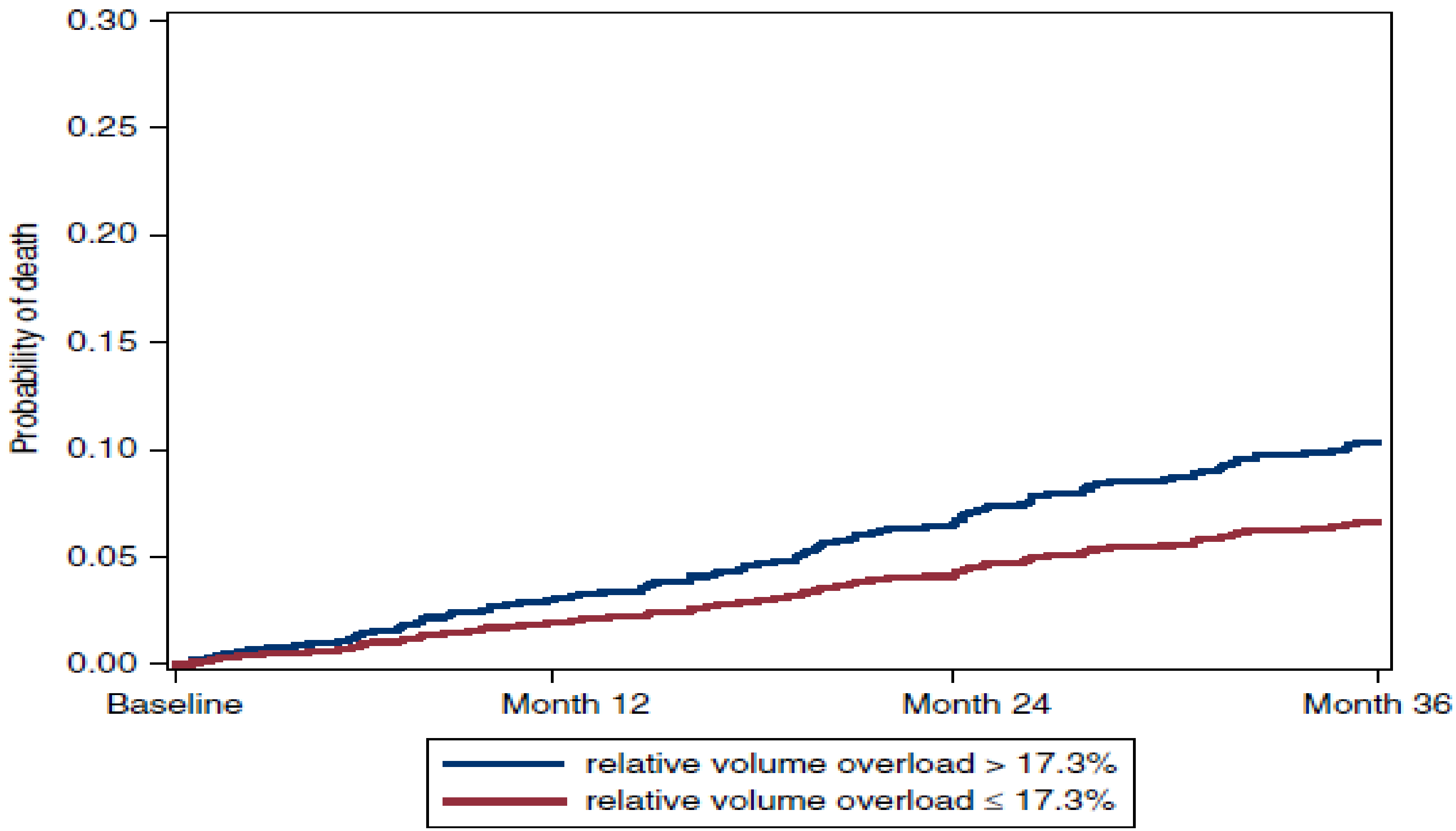
Cumulative incidence of death by volume status after initiating PD



CJASN 14: 882–893, June, 2019

Fluid Overload in Peritoneal Dialysis Patients

Yong-Lim Kim, MD, PhD, and Wim Van Biesen, MD, PhD†*

Summary: Volume management in peritoneal dialysis patients is of importance, as both volume overload and dehydration are associated with worse outcomes. When assessing volume status, it is important to understand that different techniques measure different fluid compartments (intracellular vs extracellular vs circulating volume) and the impact of cardiac function. Attention to salt restriction and diuretics can help to maintain euvolemia without need for hypertonic bags. Glycaemia should be monitored to avoid thirst. Dwell length should be adapted to transport status: short dwells for fast transporters, long dwells in slow transporters. The role of bio-compatible solutions on volume control remains controversial.
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Keywords: peritoneal dialysis, volume overload, bio-impedance, cardiac failure

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DRIVING FACTORS OF FLUID STATUS IN PD PATIENTS

1. Residual Renal Function
2. Salt and Fluid Intake
3. Inflammation and Nutritional Status
4. Small-Solute Transport
5. Impact of Dialysis Solutions
6. CAPD Versus APD

1. Residual Renal Function

- Residual renal diuresis was not related to fluid status as assessed by bioimpedance measurement in a large observational cohort of prevalent European PD patients

1. Residual Renal Function

- Absence of a consistent relation between urinary output and hydration status:
  - Output: urine, sweating, stools, and,in PD patients ultrafiltration
  - Input: fluid intake, indirectly by salt intake and control of serum glycemia
- An increased ECW/ TBW ratio was not associated with preservation of residual renal function

1. Residual Renal Function

- **Role of blockers of the RAAS axis:**
- A Cochrane analysis identified 6 open-label studies:
- Long-term (>12 mo) use of renin-angiotensin-aldosterone system blocking agents was associated with better preservation of residual renal function in patients on peritoneal dialysis as compared with other antihypertensive drug

Zhang L; Cochrane database syst rev. 2014,6

2. Salt and Fluid Intake

- **Hyperosmolarity is a main driver of thirst and thus of water intake:**
  - Salt intake
  - Poor glycemic control
- **As long as residual urinary output is maintained, the kidney will compensate the salt and fluid overload by inducing pressure diuresis**
- A high salt intake: induce changes in the peritoneal membrane

2. Salt and Fluid Intake

- **Poor glycemic control :**
  - Amplifies sodium sieving
  - Induce hyperinsulinism
  - Changes in the peritoneal membrane neoangiogenesis, leading to ultrafiltration failure

3. Inflammation and Nutritional Status

- PD patients tend to have a lower lean tissue mass and a higher fat tissue mass
- The increased ECW/TBW ratio in dialysis patients thus partly could be artificial and unrelated to true fluid overload

BRAZPD cohort. J Ren Nutr. 2013;23

3. Inflammation and Nutritional Status

- Hypoalbuminemia
  - Disturbance of the glycocalix function
  - Endothelial dysfunction
- Inflammation
  - Endotoxemia
- C-reactive protein levels
- Protein energy wasting

4. Small-Solute Transport

- **Impact of prescription:**
  - *Fluid overload was highest in patients in whom the transport status was unknown*
- An inapt prescription can cause overhydration in slow transporters
- Too short dwells can induce sodium sieving in slow transporters
- Adaptation of the dwell length to the transport status necessary to maintain normohydration

5. Impact of Dialysis Solutions

- The lower GDP containing solutions, and especially the bicarbonate-based ones, have been associated with lower vascular recruitment in rat models
- The use of neutral pH–low GDP PD solutions resulted in greater urine output and higher residual renal function when used for longer than 12 m
- **(Cochrane Database Syst Rev. 2014;3)**

5. Impact of Dialysis Solutions

Prescription of ***icodextrin*** :

- Improved peritoneal ultrafiltration
- Mitigated uncontrolled fluid overload
- Use for the long dwell increases ultrafiltration, especially in fast transporters
- The effects on the residual renal function can be variable, depending on:
  - Underlying fluid status
  - Adherence to dietary restrictions

(Cochrane Database Syst Rev. 2014;3)

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CLINICAL TRIAL/EXPERIMENTAL STUDY

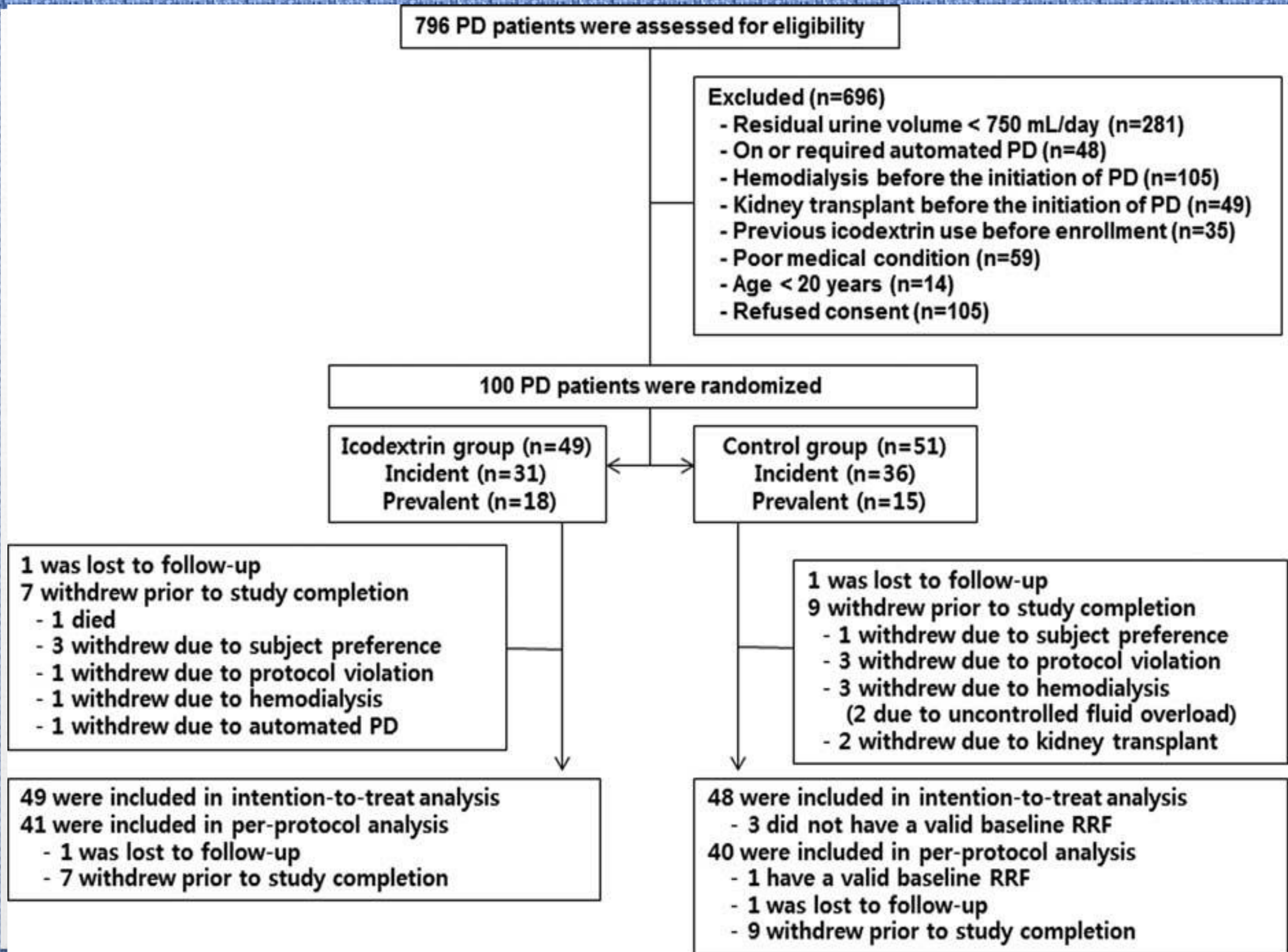
OPEN

Effect of Icodextrin Solution on the Preservation of Residual Renal Function in Peritoneal Dialysis Patients

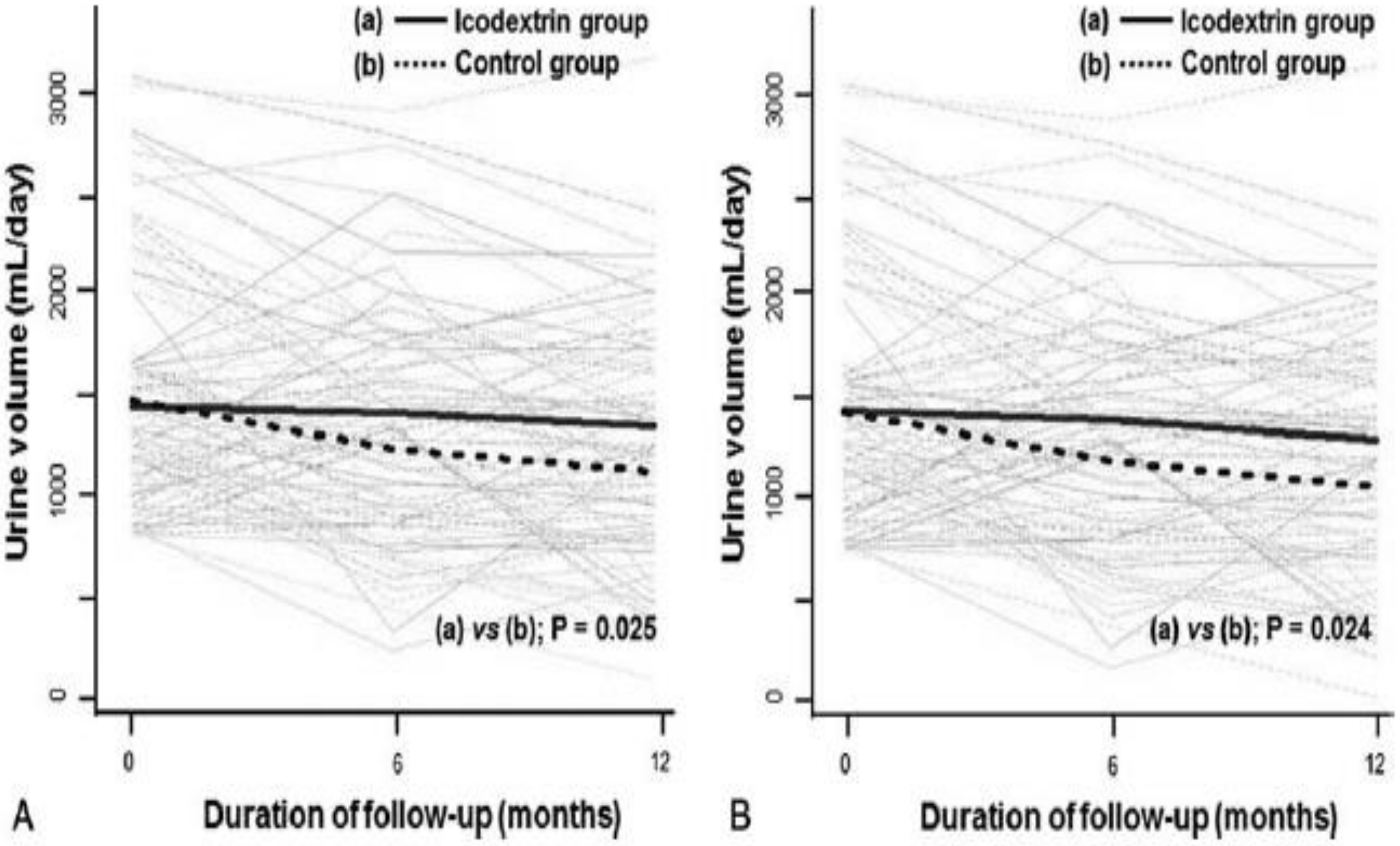
A Randomized Controlled Study

Tae Ik Chang, MD, PhD, Dong-Ryeol Ryu, MD, PhD, Tae-Hyun Yoo, MD, PhD, Hyung Jong Kim, MD, PhD, Ea Wha Kang, MD, PhD, Hyunwook Kim, MD, PhD, Jae Hyun Chang, MD, PhD, Dong Ki Kim, MD, PhD, Sung Jin Moon, MD, PhD, Soo Young Yoon, MD, PhD, and Seung Hyeok Han, MD, PhD, on behalf of the Yonsei Associate Network CHronic Kidney Disease Trial (YACHT) investigators

Medicine Volume 95, Number 13, April 2016


796 PD patients were assessed for eligibility
Excluded (n=696)
- Residual urine volume < 750 mL/day (n=281)
- On or required automated PD (n=48)
- Hemodialysis before the initiation of PD (n=105)
- Kidney transplant before the initiation of PD (n=49)
- Previous icodextrin use before enrollment (n=35)
- Poor medical condition (n=59)
- Age < 20 years (n=14)
- Refused consent (n=105)
100 PD patients were randomized
Icodextrin group (n=49)
Incident (n=31)
Prevalent (n=18)
Control group (n=51)
Incident (n=36)
Prevalent (n=15)
1 was lost to follow-up
7 withdrew prior to study completion
- 1 died
- 3 withdrew due to subject preference
- 1 withdrew due to protocol violation
- 1 withdrew due to hemodialysis
- 1 withdrew due to automated PD
1 was lost to follow-up
9 withdrew prior to study completion
- 1 withdrew due to subject preference
- 3 withdrew due to protocol violation
- 3 withdrew due to hemodialysis
(2 due to uncontrolled fluid overload)
- 2 withdrew due to kidney transplant
49 were included in intention-to-treat analysis
41 were included in per-protocol analysis
- 1 was lost to follow-up
- 7 withdrew prior to study completion
48 were included in intention-to-treat analysis
- 3 did not have a valid baseline RRF
40 were included in per-protocol analysis
- 1 have a valid baseline RRF
- 1 was lost to follow-up
- 9 withdrew prior to study completion

Prospective randomized trial showed that icodextrin solution preserves residual urine volume better than glucose solution



6. CAPD Versus APD

- No difference in sodium removal or volume control in patients on APD versus CAPD
  - If avoiding too short dwell times and sodium sieving in APD
  - Decreased sodium removal especially in patients with membranes with slower transport characteristics

Davison SN, Clin J Am Soc Nephrol. 2009;4:1044-50

EuroBCM study cohort. Plos One. 2011;6e1718

ISPD guidelines

- “hydration status should be assessed clinically on a regular basis during every follow-up visit and more often if clinically indicated”
- Hypertensive PD patients should have their volume status optimized before starting an antihypertensive treatment

ASSESSMENT OF FLUID STATUS

- A need for formal assessment of fluid status:
- Clinical observation alone is insufficient
  - Low sensitivity for overhydration
- Up to 30% of patients who are labeled as normohydrated appear to be overhydrated when a formal assessment is performed

How to assess fluid status

- Inferior vena cava diameter
- Biomarkers
- Lung ultrasound
- Bioelectrical impedance techniques

Inferior vena cava diameter

- Measurement of the diameter of inferior vena cava (IVC) and its decrease on deep inspiration (collapsibility index—CI) by echocardiography allows an accurate assessment of dry weight in hemodialysis patients
- Estimates only intravascular volume

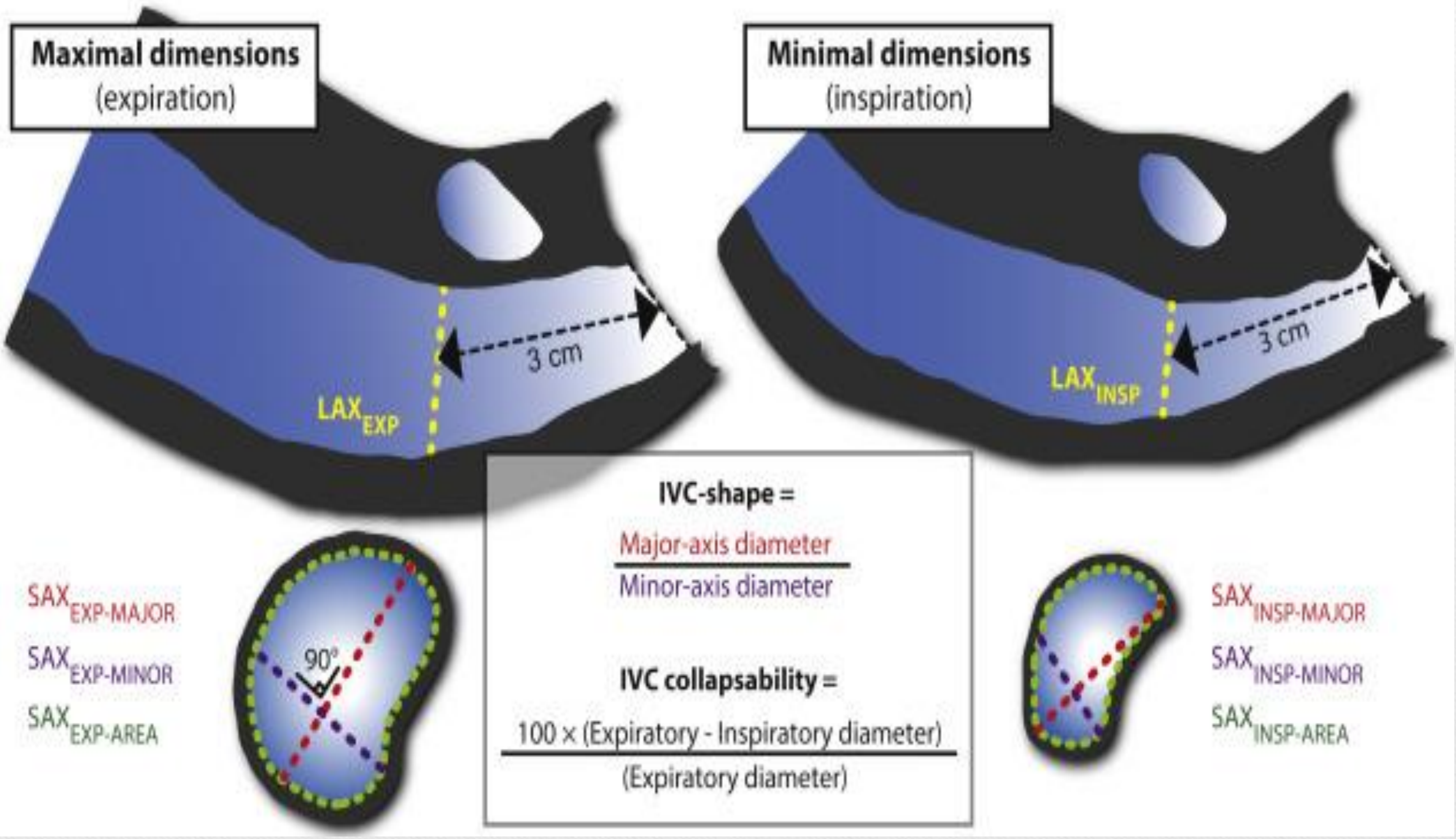
Inferior vena cava diameter

- In PD populations, the IVC diameter, especially maximal diameter in quiet expiration (IVC_e), significantly correlates with:
  - Cardiothoracic ratio
  - Plasma ANP concentration
- IVC index is a useful tool for assessing the volume status in PD patients and an independent predictor of left ventricular geometric stratification

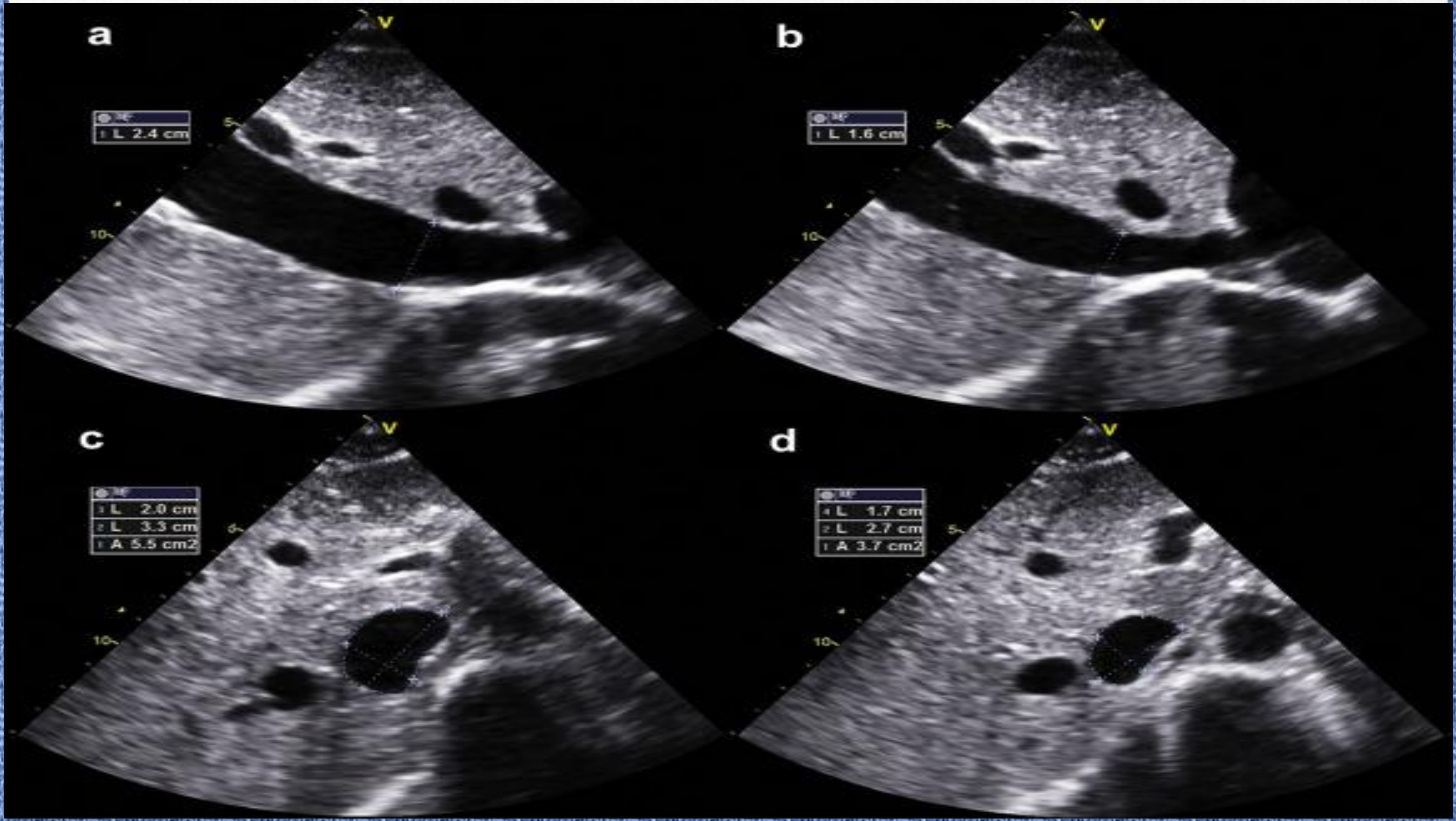
Some caveats should be kept in mind

- Wide variation of IVC diameters in healthy individuals, and single measurements are not helpful
- A significant, inverse correlation between IVC diameters and heart rate
  - Intravascular volume assessment is improved by correcting for the heart rate
  - The presence of tricuspid insufficiency leads to unreliable results

Schematic of inferior vena cava measurements during expiration (left) and inspiration (right)



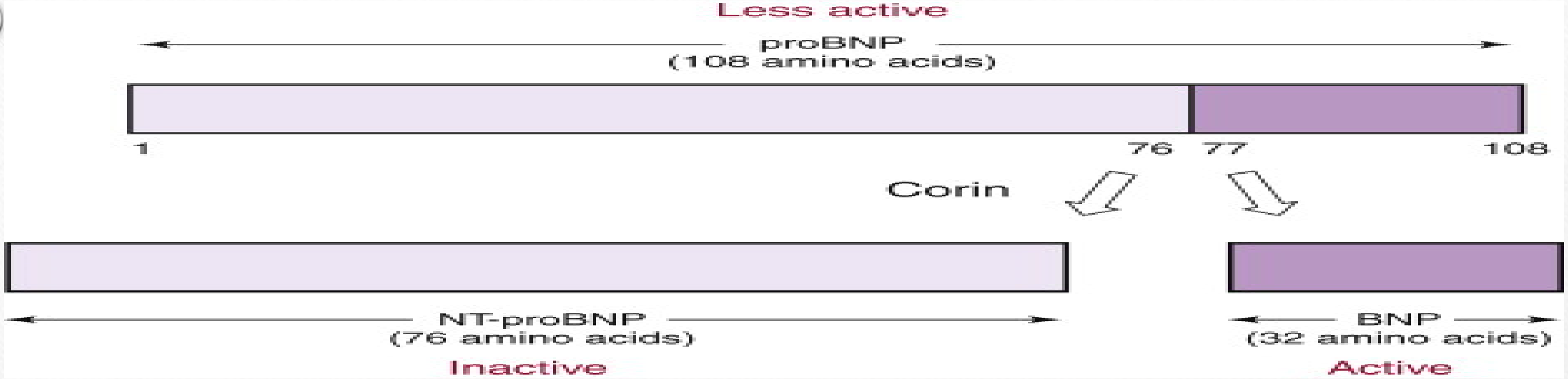
Echocardiographic views of long-axis (a, b) short-axis (c, d) maximal expiratory (a, c) minimal inspiratory (b, d) inferior vena cava



Biomarkers

BNP

- Released primarily by the ventricular myocytes
- Reflects filling pressure of the left atrium
- A prognostic indicator for mortality
- A marker of fluid status
- Partly is cleared by dialysis and to a small extent by the kidneys
- In PD is a good reflection of right ventricular end-diastolic pressure



- In PD:
  - Plasma BNP and NT pro-BNP levels are elevated and correlate with volume overload
- In ADEMEX study, only NT-proBNP levels alone, predictive of overall survival and cardiovascular mortality of PD patients, independent of volume overload

Cardiac troponins T and I (cTnT and cTnI)

- Subunits of the cardiac actin–myosin complex
- Sensitive and specific marker of myocardial cell necrosis
- Associated with mortality in HD and CAPD
- NT-proBNP > cTnT and hsCRP : significant prognostic factor for cardiovascular mortality
- hsCRP > NT-proBNP and cTnT : significant predictor for all-cause mortality
- <u>Their elevated levels independently identify a greater risk for death, but they cannot assess volume status</u>

Lung Ultrasound

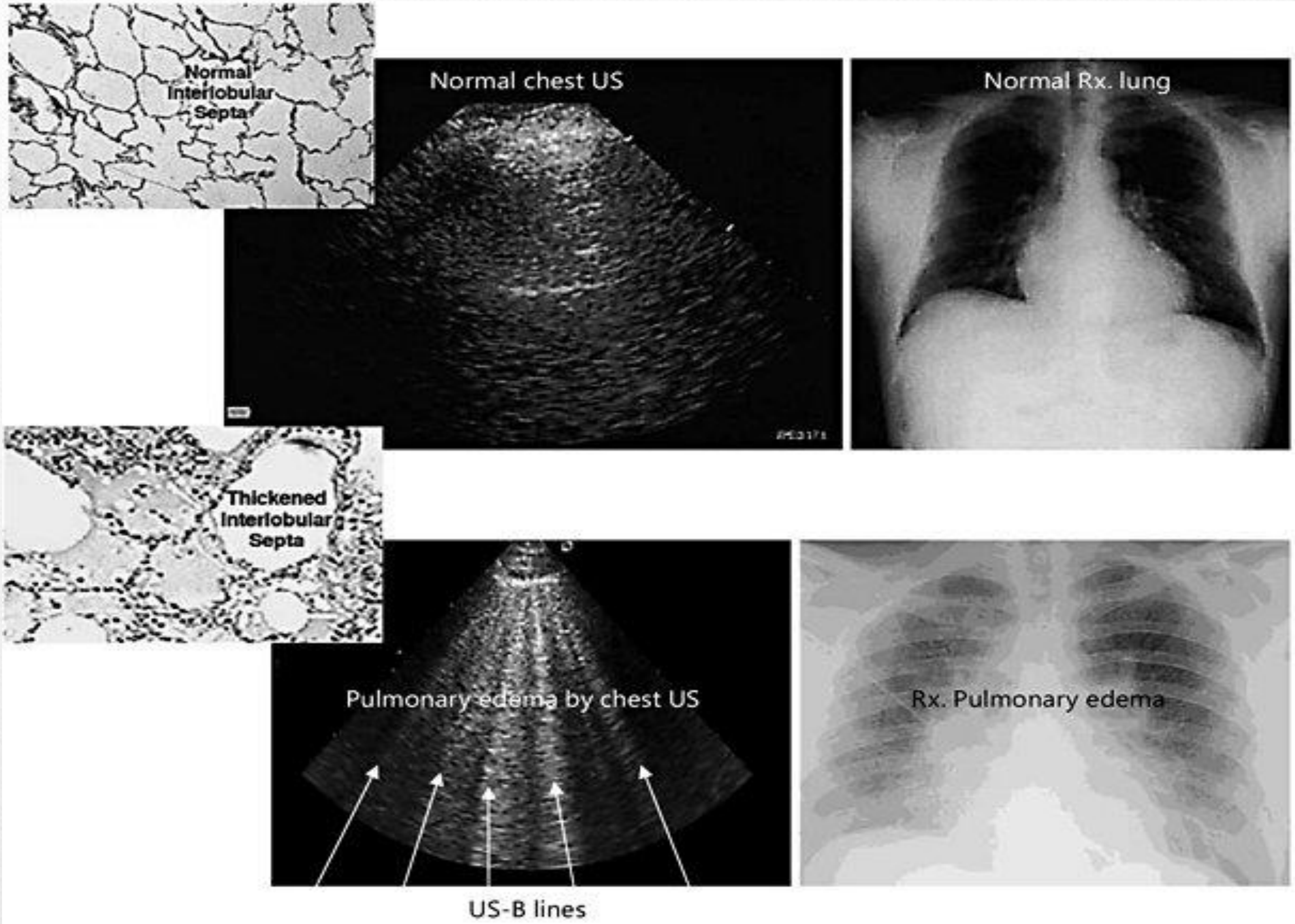
Lung Ultrasound

- It is a novel, reproducible validated technique
- Estimate lung water in ESRD patients
- Ultrasound beam is reflected by thickened interlobular septa, generating hyperechoic artifacts between edematous septa and the overlying pleura (the so-called lung comets)
- The number of these lung comets is associated with left ventricular filling pressure

Lung Ultrasound

Panuccio V, Nephrol Dial Transplant. 2012; 3601-5

- Assess the extravascular water content of the lungs
- A semiquantitative appreciation of the presence of reflections (called *comets*)
- Reflects pulmonary wedge pressure
- Left ventricular preload and circulating volume in relation to cardiac function rather than fluid status

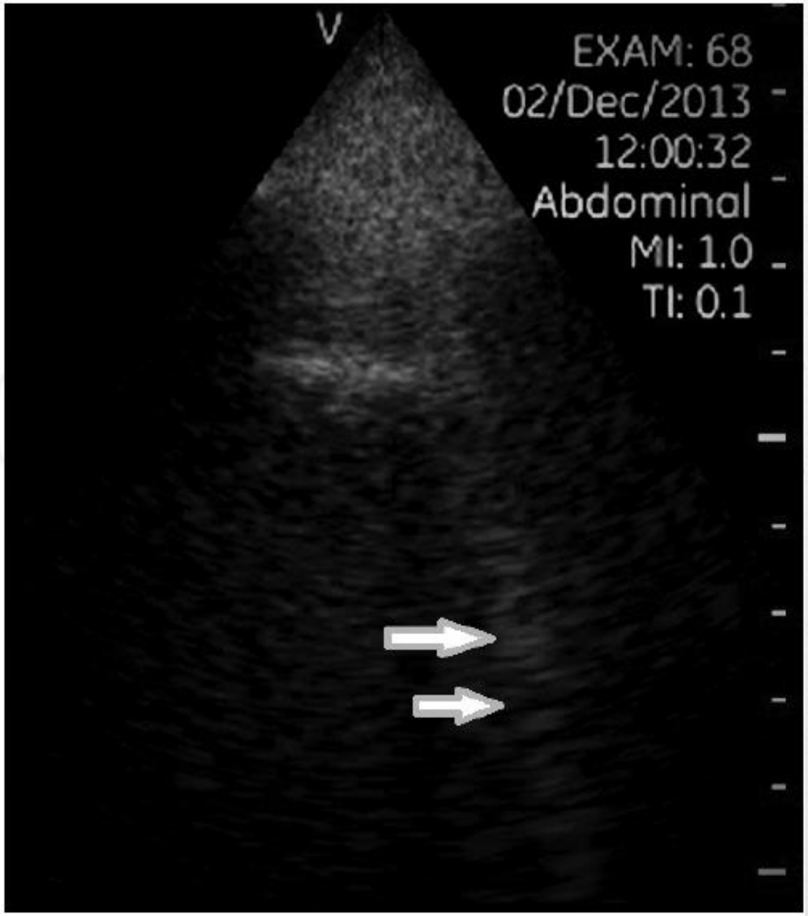


Blood Purif 2013;36:184–191

Lung Ultrasound

- The number of these lung comets is associated with left ventricular filling pressure
- Lung water excess was mainly associated with (NYHA) functional class

Zoccali C, J Am Soc Nephrol.2013;24(4):639–46



Comet score

- **mild congestion:**
  <14 comets
- **moderate congestion:**
  ≥14 to ≤30 comets
- **severe congestion:**
  >30 comets

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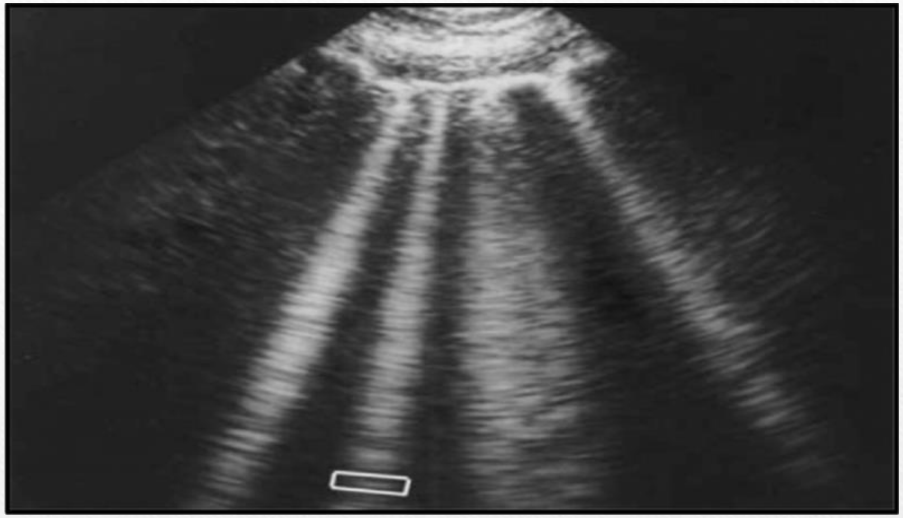


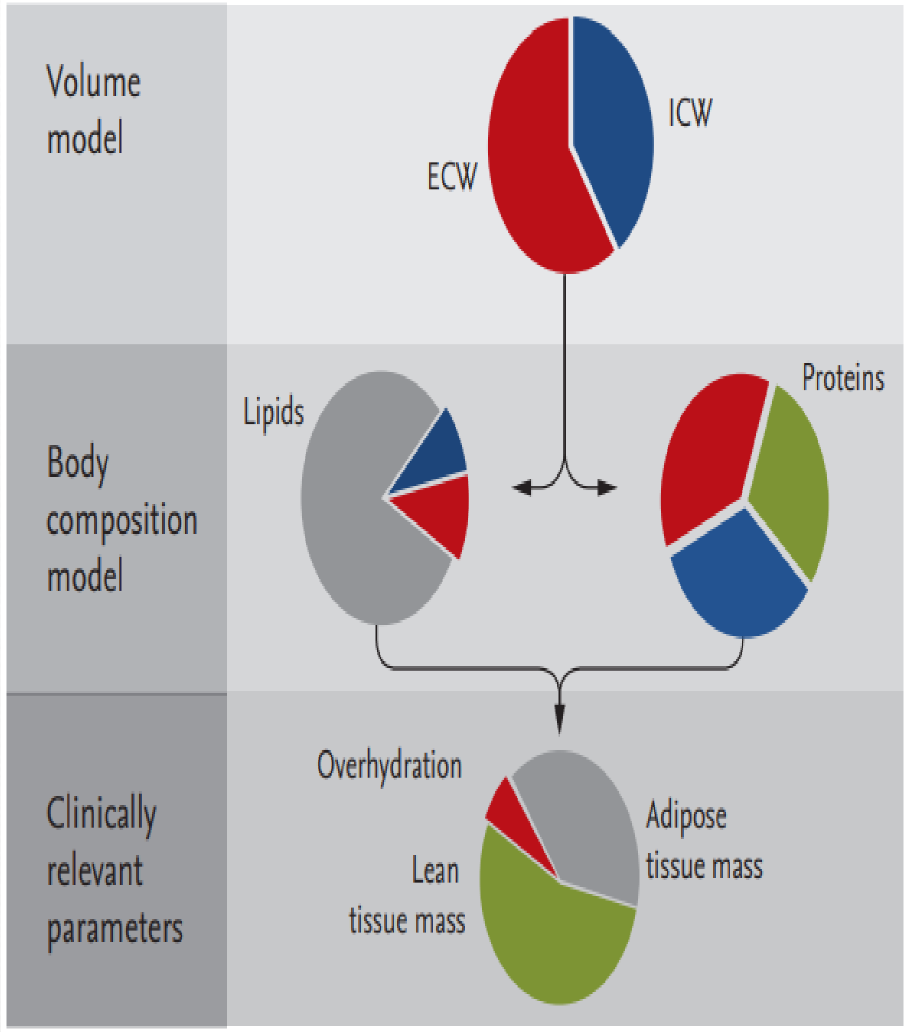
Bioelectrical impedance techniques

- **Bioimpedance techniques:**
  - Pass a low-strength alternating current into the body, and biological tissues react to the flow according to the current frequency and the properties of the tissue (this is called impedance)

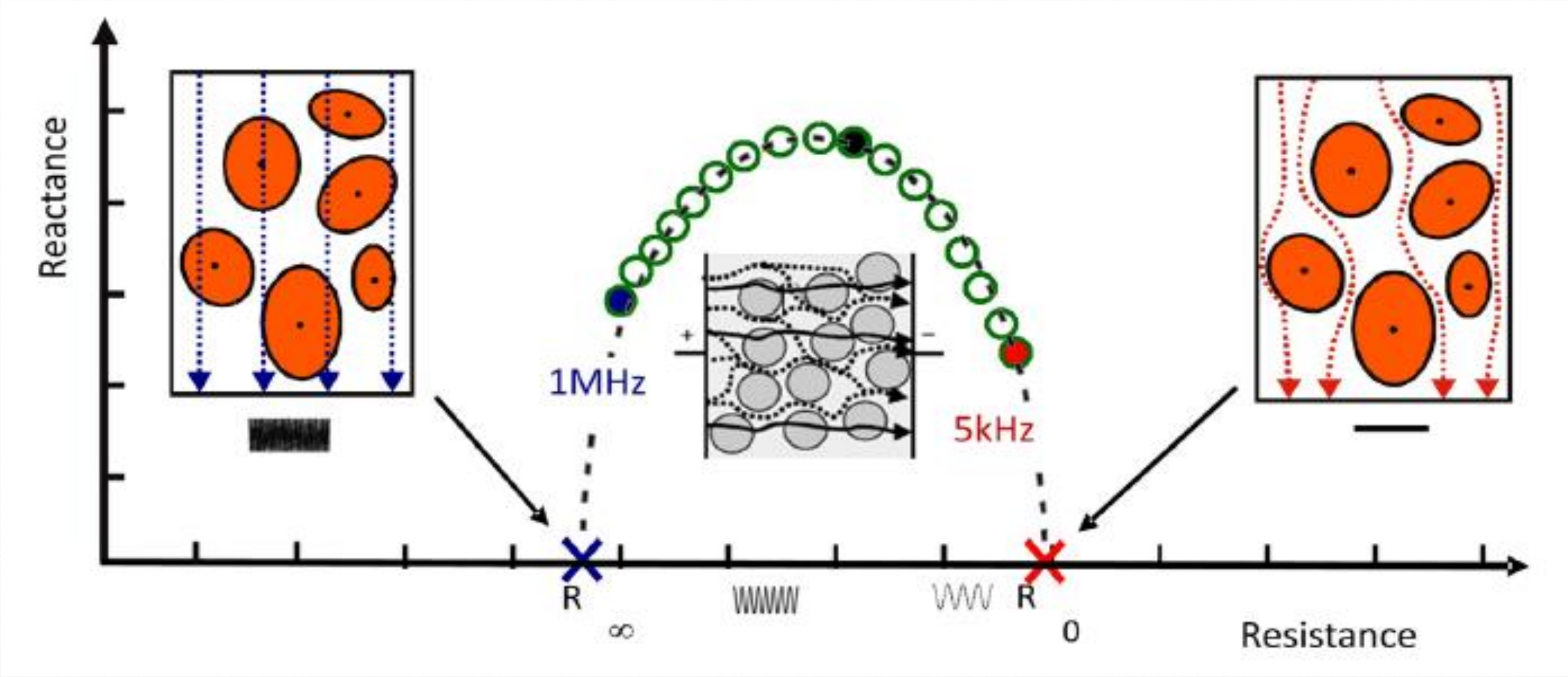
- The two basic properties of impedance :
  - **Resistance**
    - Flow of the electrons through the tissue
      - The amount of fluid
  - **Capacitance**
    - How much energy is stored and released in each current alternating cycle
      - The cell mass

The volume model describes electrical conductance in a cell suspension enabling the TBW, ECW, and ICW to be calculated

The body composition model is used for calculating the three relevant body compartments, namely overhydration, lean tissue, and adipose tissue, from ECW and TBW information



- **Low-frequency currents** (<5 kHz) pass through the ECV (they cannot pass the cell membrane)
- **High frequency currents** pass through both ECV and ICV compartments

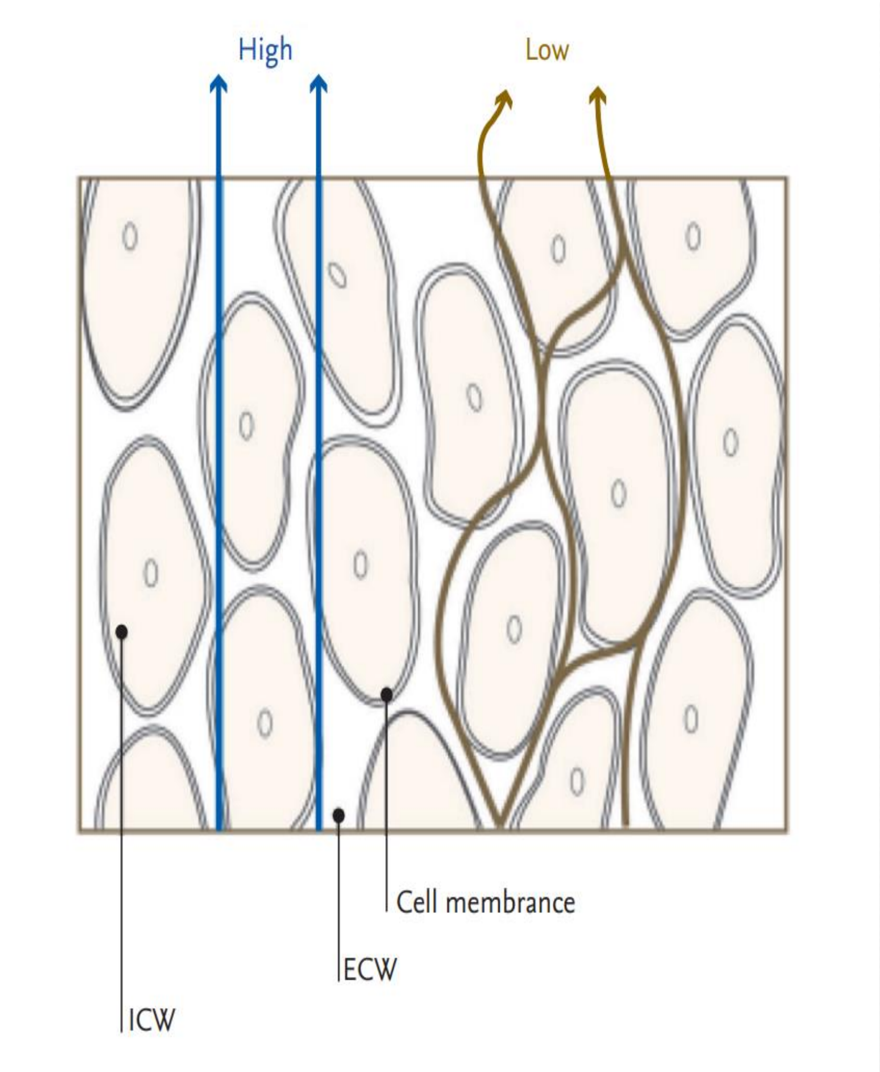


Zero frequency : Only extracellular paths contributes

Low frequency : Extracellular current paths dominate

Intermediate frequency : Intracellular current paths partially contribute

Infinite frequency : : Intracellular current paths additionally contribute



Current flows in tissue at low and high frequencies

BIA

- Bioimpedance has been linked to mortality both in HD as in PD
- BIA is good to identify changes in fluid status that otherwise might not be clinically identifiable
- Allows assessment of ECW, ICW, and TBW

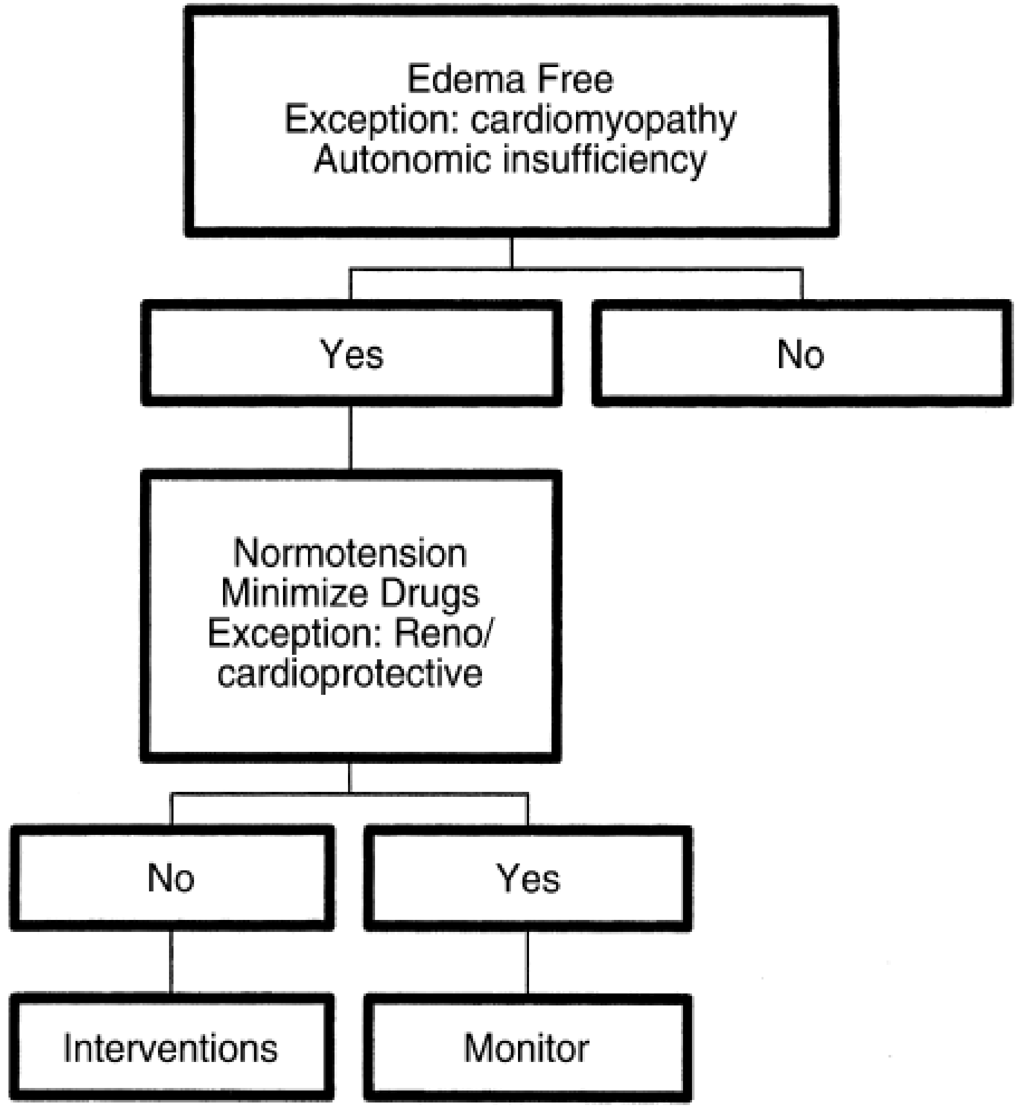
Limitations of BIS methods in PD populations

- First, the ratio ECW/TBW is disproportionally increased due to absolute reduction in tissue mass, mainly muscle mass and abnormal tissue hydration
- Secondly, absolute values of BIS measurements are based on equations derived from healthy populations
- Finally, BIS cannot discriminate intravascular vs extravascular volume

Technique	What is estimated	Advantages	Limitations
Dilution tracers	ECV, TBW	Gold standard method	Invasive, not for everyday clinical practice
IVC	Intravascular filling–BV	Correlation with cardiac Function, noninvasive	Experienced cardiologist
Bioimpedance	ECV, ICV, TBW	Easy, noninvasive, fluid volumes in liters	No standardization Influenced by hypoalbuminemia and muscle wasting
Biomarkers	Intravascular filling–BV	Noninvasive	Wide variability Influenced by cardiac dysfunction
Lung ultrasound	Intravascular filling–BV	Noninvasive, easy	No estimation of TBW, ECV Little experience in PD

IVC, inferior vena cava diameter; ECV, extracellular volume; ICV, intracellular volume; TBW, total body water; BV, blood volume.

fluid management in patients on PD



STRATEGIES TO ACHIEVE EUVOLEMIA IN PD PATIENTS

Strategies to improve Volume Management in PD

- Start PD earlier
- Protect residual renal function
- Use high-dose loop diuretics o maintain urine output
- Educate patients regarding salt and water intake and regarding significance of oedema, weight gain, etc
- Appropriate use of hypertonic solutions
- Awareness of PET status

Strategies to improve Volume Management in PD

- Consider APD in high and high average transporters
- Night exchange device in CAPD
- Short day dwells on APD – long enough to give good clearance and short enough to give good UF
- Icodextrin for long dwells in CAPD & APD
- Frequent reassessment of the patient’s target weight
- Anti-hypertensives only when volume removal has failed to reduce BP