Hemodialysis & Peritoneal dialysis: Adequacy Issues

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김 도 형

Adequacy

- Adequate dialysis
  - Effective dosage of dialysis solution capable of keeping a patient clinically asymptomatic and active and maintaining a good enough correction of the altered metabolic and homeostatic components secondary to the loss of kidney function.

- Optimal dialysis
  - The dose capable of reducing morbidity and mortality associated with ESRD and with the dialytic procedure itself
  - The dose above which an increase does not justify the greater burden of treatment

Clinical criteria for adequate dialysis

- Subjective
  - Feeling of well-being
  - Absence of uremic symptoms

- Objective
  - Reasonable control of biochemical parameters
  - Anemia control
  - Euvolemic state (absence of congestion, peripheral edema)
  - Normotension or good BP control
Adequate dialysis

- Solute clearance
- Uremic Toxins
- Electrolytes Regulation
- Acid-base Balance
- Ca-P control
- Volume homeostasis
- Fluid Overload
- BP control

An adequately treated dialysis patient is physically active, well nourished, euvoletic and normotensive, with a maintained good quality of life and a life expectancy that is not inferior to that of healthy patients.

Adequacy evaluation: $Kt/V_{urea}$

- **Urea**
  - End product of protein intake, catabolism by the liver
  - Generation: not constant (meat intake, GI bleeding, etc.)
  - Traditional solute to quantitate dialysis
  - Low molecular weight: 60Da
    - rapid diffusion between body compartments
    - application of a single-pool model for approximation

- $Kt/V_{urea}$
  - Fractional clearance of urea
  - Clearance of urea ($K$) per time unit ($t$) in relation to its volume of distribution or total body water ($V$)

Adequacy evaluation: $Kt/V_{urea}$

- **Kt / Vurea**
  - HD: membrane clearance
  - PD: daily peritoneal urea clearance
  - $V$: total body water

- **K**: clearance
- **t**: time
- **V**: total body water, $Kt/V$: unit-less

- **V (by Watson formula)**
  - $V = 2.447 - 0.095616 \times A + 0.1704 \times H + 0.3382 \times W$ (in males)
  - $V = 2.097 + 0.1069 \times H + 0.2496 \times W$ (in females)
  - $A =$ age (y), $H =$ height (cm), and $W =$ weight (kg)*

*median standard or ideal body weight instead of actual body weight

Handbook of dialysis 8th Ch. 28
HD Adequacy

- Urea reduction ratio
  \[ \text{Urea reduction ratio} = \frac{(\text{BUN}_{\text{preT}} - \text{BUN}_{\text{postT}})}{\text{BUN}_{\text{preT}}} \times 100 \]

- \( k_t/V_{\text{urea}} \)
  - \( K \): Urea clearance of dialyzer (mL/min)
  - \( K_{\text{oA}} \): Dialyzer efficiency
  - \( Q_b \): Blood flow rate
  - \( Q_{\text{d}} \): Dialysate flow rate
  - \( t \): Time of dialysis session (min)
  - \( V \): Volume of urea distribution ≈ Total body water (mL)

- "\( k_t/V = 1 \)" means "One Turn"
  - Total blood volume cleared during the dialysis session = TBW
  - "Whole volume was passed once through the dialyzer"

Definition of \( k_t/V \) - HD

- Single-pool \( k_t/V \) (sp\( k_t/V \))

- Equilibrated \( k_t/V \) (e\( k_t/V \))

- Standard \( k_t/V \) (std\( k_t/V \))
Single-pool Kt/V (spKt/V)

\[ \text{Kt/V} = 1 - R = \text{URR} \]
\[ R = \text{post BUN/pre BUN} \]
\[ T = \text{Time (hr)} \]
\[ UF = \text{ultrafiltration weight} \]
\[ W = \text{postdialysis weight} \]

\[ \text{spKt/V} = \frac{- \ln(R - 0.008xT) + (4 - 3.5 \times R) \times UF/W}{\text{adjust for urea generation and volume reduction}} \]

Equilibrated Kt/V (eKt/V)

- eKt/V is an equation considering urea rebound caused by urea diffused back from sequestered tissues
- Usually lower than spKt/V by 0.15 – 0.20
  - eKt/V = spKt/V – 0.6(spKt/V) / t + 0.03 (arteriovenous access)
  - eKt/V = spKt/V – 0.47 (spKt/V) / t + 0.02 (venous access)

Standard Kt/V (stdKt/V)

- Hypothetical continuous clearance in patients treated with intermittent hemodialysis based on the generation rate of urea nitrogen and the average predialysis urea nitrogen

\[ \text{stdKt/V} = \frac{10.080}{1 - \text{Kt/V} + 10.080 \times \text{Kt/V}} \]

\[ \text{stdKt/V} = \frac{S}{1 - 0.74 \times \frac{Kt}{V}} + Kt \cdot 10.80 \times \frac{V}{V} \]

- S: the number of dialyses per week
- UF: the weekly ultrafiltration volume in mL
- V: the volume of ultrafiltration in mL
- Kt: the residual native kidney clearance of urea in mL/min
- 10,080: the number of minutes in a week

Guideline 1: Timing of Hemodialysis Initiation

1.1 Patients who reach CKD stage 4 (GFR < 30 mL/min/1.73 m²), including those who have imminent need for maintenance dialysis at the time of initial assessment, should receive education about kidney failure and options for its treatment, including kidney transplantation, PD, HD in the home or in-center, and conservative treatment. Patients’ family members and caregivers also should be educated about treatment choices for kidney failure. (Not Graded)

1.2 The decision to initiate maintenance dialysis in patients who choose to do so should be based primarily upon an assessment of signs and/or symptoms associated with uremia, evidence of protein-energy wasting, and the ability to safely manage metabolic abnormalities and/or volume overload with medical therapy rather than on a specific level of kidney function in the absence of such signs and symptoms. (Not Graded)


Guideline 2: Frequent and Long Duration Hemodialysis

- In-center Frequent HD

2.1 We suggest that patients with end-stage kidney disease be offered in-center short frequent hemodialysis as an alternative to conventional in-center thrice weekly hemodialysis after considering individual patient preferences, the potential quality of life and physiological benefits, and the risks of these therapies. (2C)

2.2 We recommend that patients considering in-center short frequent hemodialysis be informed about the risks of this therapy, including a possible increase in vascular access procedures (1B) and the potential for hypotension during dialysis. (1C)

Guideline 2: Frequent and Long Duration Hemodialysis

- Home Long HD

2.3 Consider home long hemodialysis (6-8 hours, 3 to 6 nights per week) for patients with end-stage kidney disease who prefer this therapy for lifestyle considerations. (Not Graded)

2.4 We recommend that patients considering home frequent hemodialysis be informed about the risks of this therapy, including possible increase in vascular access complications, potential for increased caregiver burden, and possible accelerated decline in residual kidney function. (1C)

- Pregnancy

2.5 During pregnancy, women with end-stage kidney disease should receive long frequent hemodialysis either in-center or at home, depending on convenience. (Not Graded)


Guideline 3: Measurement of Dialysis—Urea Kinetics

3.1 We recommend a target single pool Kt/V (spKt/V) of 1.4 per hemodialysis session for patients treated thrice weekly, with a minimum delivered spKt/V of 1.2. (1B)

3.2 In patients with significant residual native kidney function (Knu), the dose of hemodialysis may be reduced provided Knu is measured periodically to avoid inadequate dialysis. (Not Graded)

3.3 For hemodialysis schedules other than thrice weekly, we suggest a target standard Kt/V of 2.3 volumes per week with a minimum delivered dose of 2.1 using a method of calculation that includes the contributions of ultrafiltration and residual kidney function. (Not Graded)

- Methods for Measuring Urea Clearance

The predialysis blood sample must be drawn before injecting saline, heparin, or other potential diluents.

The post-dialysis blood sample should be drawn from the dialyzer inflow port using a slow-flow method (100 mL/min for 15 seconds) or a stop–dialyzer–flow method (for 3 minutes). These measurements should be done at least monthly as recommended in the previous guidelines.


Guideline 4: Volume and Blood Pressure Control—Treatment Time And Ultrafiltration Rate

4.1 We recommend that patients with low residual kidney function (<2 mL/min) undergoing thrice weekly hemodialysis be prescribed a bare minimum of 3 hours per session. (1D)

4.1.1 Consider additional hemodialysis sessions or longer hemodialysis treatment times for patients with large weight gains, high ultrafiltration rates, poorly controlled blood pressure, difficulty achieving dry weight, or poor metabolic control (such as hyperphosphatemia, metabolic acidosis, and/or hyperkalemia). (Not Graded)

4.2 We recommend both reducing dietary sodium intake as well as adequate sodium/water removal with hemodialysis to manage hypertension, hypervolemia, and left ventricular hypertrophy. (1B)

4.2.1 Prescribe an ultrafiltration rate for each hemodialysis session that allows for an optimal balance among achieving euvoledia, adequate blood pressure control and solute clearance, while minimizing hemodynamic instability and intradialytic symptoms. (Not Graded)


- 6 -
Guideline 5: Hemodialysis Membranes

5.1 We recommend the use of biocompatible, either high or low flux hemodialysis membranes for intermittent hemodialysis. (1B)

<table>
<thead>
<tr>
<th>Guidelines</th>
<th>KDOQI (2015)</th>
<th>Renal association (UK)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodialysis</td>
<td>Minimum spKt/V 1.2 per session,</td>
<td>Consistently eKt/V &gt; 1.2 or spKt/V &gt; 1.3</td>
</tr>
<tr>
<td>(for thrice weekly dialysis)</td>
<td>target spKt/V 1.4 per session</td>
<td>Minimum target eKt/V at least 1.3</td>
</tr>
<tr>
<td></td>
<td>Recommends phasing out URR</td>
<td>Consistently URR&gt;65% or</td>
</tr>
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<td></td>
<td></td>
<td>Minimum target URR of 70%</td>
</tr>
<tr>
<td>RKF in HD</td>
<td>Quarterly measurements advised.</td>
<td>Suggest employing strategies to preserve RKF. i.e., reduce intradialytic</td>
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<tr>
<td></td>
<td>Dose of dialysis can be reduced in</td>
<td>hypotension</td>
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<tr>
<td></td>
<td>patients with significant RKF</td>
<td>Twice weekly HD may be acceptable if patients have a combined urea and</td>
</tr>
<tr>
<td></td>
<td>(should then be measured monthly)</td>
<td>creatinine clearance or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>eGFR of 5 mL/min/1.73 m²</td>
</tr>
</tbody>
</table>

Management of low Kt/V in HD

Comprehensive clinical nephrology 4th Ch. 90
PD Adequacy

Criteria for Peritoneal Dialysis Adequacy

| Clinical | Patient feels well and has stable lean body mass  
|          | No symptoms of anorexia, asthenia, nausea, emesis, insomnia  
|          | Stable nerve conductance velocity  
| Small-solute clearance | Weekly Kt/V urea >1.7 (renal + peritoneal)  
|                | Weekly creatinine clearance >50 V1.73 m²  
| Large-solute clearance | Albumin clearance <0.15 m/m/min  
| Fluid balance | No edema  
|                | No hypertension  
|                | No postural hypotension  
| Electrolyte balance | Serum potassium <5 mmol/l  
| Acid-base balance | Serum bicarbonate >24 mmol/l  
| Nutrition | Daily protein intake ≥1.2 g/kg  
|                | Daily calorie intake ≥35 kcal/kg/day  
|                | Serum albumin ≥3.5 g/l  
|                | BMI 20–30 kg/m²  
|                | Stable midarm muscle circumference

PD adequacy

- Traditional markers of PD adequacy: small solute clearance
- Kt/Vare: urea clearance corrected for total body water
- CrCl: creatinine clearance normalized to 1.73 m² BSA
**Kt/V_{urea}**: Fractional Clearance of Urea

- **K**: clearance \( t \): time \( V \): total body water, \( Kt/V \): unit-less

- **Kt** = total \( Kt \) = peritoneal \( Kt \) + renal \( Kt \)
  - Peritoneal \( Kt \) = 24hr dialysate urea nitrogen content/serum urea nitrogen
  - Renal \( Kt \) = 24hr urine urea nitrogen content/serum urea nitrogen

- **V** (by Watson formula)
  - \( V = 2.447 - 0.09516A + 0.1704H + 0.3362W \) (in males)
  - \( V = -2.057 + 0.1069H + 0.2466W \) (in females)
  - \( A = \text{age} \) (y); \( H = \text{height} \) (cm), and \( W = \text{weight} \) (kg)²
  - median standard or ideal body weight instead of actual body weight

- **Weekly Kt/V_{urea}** = 7days \( \times (\text{peritoneal} \ Kt + \text{renal} \ Kt)/V \)

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**Creatinine clearance**

- **CrCl** = total \( \text{CrCl} \) corrected for 1.73 m² BSA
- **Total CrCl** = peritoneal \( \text{CrCl} \) + renal \( \text{CrCl} \)
  - Peritoneal \( \text{CrCl} \) = 24hr dialysate creatinine content/serum creatinine
  - Renal \( \text{CrCl} \) = 0.5 \( \times \) (24hr urine creatinine content/serum creatinine + 24hr urine urea nitrogen content/serum urea nitrogen)

  *For PD adequacy purposes, renal ‘CrCl’ is the average of the urinary creatinine and urea clearances.

- Urea clearance: tubular reabsorption : GFR underestimation
- Creatinine clearance: tubular secretion: GFR overestimation
- \( \text{BSA (DuBois formula (m²))} = 0.007184 \times W^{0.425} \times H^{0.725} \)
  - \( \text{BSA} = \text{body surface area (m²)} \), \( W = \text{weight (kg)}² \) and \( H = \text{height (cm)} \)
  - median standard or ideal body weight instead of actual body weight

- **Weekly CrCl** = 7days \( \times (\text{peritoneal} \ \text{CrCl} + \text{renal} \ \text{CrCl}) \times 1.73/\text{BSA (L/week/1.73m²)}

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**Creatinine clearance**

- The idea of setting a separate creatinine target
  - Model a uremic toxin that had slightly higher molecular weight than urea (113 vs. 60 Da)
  - Not so rapidly removed by diffusion

- Most current guidelines no longer recommend a minimum level of weekly \( \text{CrCl} \)
  - Weekly \( \text{CrCl} \) targets have not been shown to be of any additional value over \( Kt/V \) Targets.

- Analytical problem in measuring creatinine in glucose-containing dialysate
  - Artifically elevate the measurement of Cr -> Need correction factor
  - Each laboratory should make a correction for this based on its own experience
# PD adequacy

- The proportion of total body water (distribution space of urea) of which urea is cleared per unit time

- **Kt/V urea**
  - **Kt** = total **Kt** = peritoneal **Kt** + renal **Kt**
    - Peritoneal **Kt** = 24hr dialysate urea nitrogen content/serum urea nitrogen
    - Renal **Kt** = 24hr urine urea nitrogen content/serum urea nitrogen
  - **Weekly Kt/V urea** = 7 days x (peritoneal **Kt** + renal **Kt**) / V

- **Creatinine clearance**
  - **CrCl** = total **CrCl** corrected for 1.73 m² BSA
  - **Total CrCl** = peritoneal **CrCl** + renal **CrCl**

## Adequacy evaluation process

- **Dialysate**
  - 24hr dialysate collection, mix well, about 20cc sampling
  - Measurement: urea, creatinine, total volume

- **Urine**
  - 24hr urine collection
  - Refrigeration of specimen at +4-8°C with preservation to prevent bacterial breakdown of urea
  - Measurement: urea, creatinine, total volume

- **Serum**
  - Timing of sample
    - CAPD: anytime
    - APD: middle of the noncycling daytime period
  - Measurement: urea, creatinine

- Height, body weight

## PD solute clearance target (1)

2.1 For patients with RKF (considered to be significant when urine volume is > 100 mL/d):

2.1.1 The **minimal** “delivered” dose of total small-solute clearance should be a total (peritoneal and kidney) **Kt/V urea** of at least 1.7 per week. (B)

2.1.2 Total solute clearance (residual kidney and peritoneal, in terms of **Kt/V urea**) should be measured within the first month after initiating dialysis therapy and at least once every 4 months thereafter. (B)

2.1.3 If the patient has greater than 100 mL/d of residual kidney volume and residual kidney clearance is being considered as part of the patient’s total weekly solute clearance goal, a 24-hour urine collection for urine volume and solute clearance determinations should be obtained at a **minimum of every 2 months**. (B)
2.2 For patients without RKF (considered insignificant when urine volume is ≤100 mL/d):
2.2.1 The *minimal* "delivered" dose of total small-solute clearance should be a *peritoneal Kt/V_{true} of at least 1.7 per week measured within the first month after starting dialysis therapy and at least once every 4 months thereafter. (B)
**Frequency of measurements**

<table>
<thead>
<tr>
<th></th>
<th><strong>Kt/Vurea</strong></th>
<th><strong>Urinary clearance</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>KDOQI</strong></td>
<td>• Within 1 month of initiating PD</td>
<td>• Within 1 month of initiating PD</td>
</tr>
<tr>
<td></td>
<td>• Every 4 months</td>
<td>• Minimum of every 2 months</td>
</tr>
<tr>
<td></td>
<td>• Every significant change in the PD prescription</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• The patient's clinical status</td>
<td></td>
</tr>
<tr>
<td><strong>ISPD</strong></td>
<td>-</td>
<td>• Every 1–2 months if practicable, otherwise no less frequently than every 4–6 months</td>
</tr>
<tr>
<td><strong>CRC-ESRD</strong></td>
<td>• 후식시적 혈당 전후로 시험, 6개월 간격으로 측정</td>
<td>• 가능하다면 전여성기능을 최소한 1-2달에 한 번씩 측정</td>
</tr>
<tr>
<td></td>
<td>• 전여성기능이나 임상적인 변화가 발생하면 추가측정 필요</td>
<td>• 다르면 3-4개월에 한 번씩은 전여성기능 측정</td>
</tr>
<tr>
<td></td>
<td>• 전여성기능이 빠르게 감소한다면, 투석액 Kt/V가 1.7 미만으로 유지되는 환자에서 전여성 Kt/V은 매 3-6개월마다 측정을 권장</td>
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</tbody>
</table>

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**Seminars in Dialysis**

**MISTAKES WE MAKE IN DIALYSIS**

We Use Kt/V Urea as a Measure of Adequacy of Peritoneal Dialysis

Joanne M. Bargman
Division of Nephrology, University Health Network, Toronto, Ontario

- Another metric to gauge adequacy of dialysis remains elusive, and a single test may never be able to capture such a complex process.
- We need to keep looking at and listening to our patients, and remain vigilant about systemic inflammation, nutrition, and fluid volume status.

Seminars in Dialysis—Vol.25, No 4 (July-August) 2016

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**Factors Determining Clearance PD patients**

- **Patient-related factors**
  - Residual renal function
  - Body size
  - Peritoneal transport characteristics

- **Prescription-related factors**
  - **CAPD**
    - Dwell volume
    - Frequency of exchanges
    - Tonicity of dialysis solution
  - **APD**
    - Number of day dwells
    - Volume of day dwells
    - Tonicity of day dwells
    - Time on cycler
    - Cycle frequency
    - Cycler dwell volumes
    - Tonicity of cycler solution

Handbook of dialysis 8th Ch. 26
Clinical features that need to increase clearance

- 요독증성이 발생하거나 임상적인 증상이 악화된다고 판단되는 경우, 말기신부전 의의 다른 원인이 없다면 종 Kt/V, crea가 권고수준 이상이 되더라도 투석량을 용려야 한다(근거 수준 II, 권고수준 B).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>투석종양을 증가시켜야 할 투석양상의 예</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) 설열이 되지 않는 구역과 구토 증상</td>
<td></td>
</tr>
<tr>
<td>2) 수면장애</td>
<td></td>
</tr>
<tr>
<td>3) 가사혈중</td>
<td></td>
</tr>
<tr>
<td>4) 고혈압혈증</td>
<td></td>
</tr>
<tr>
<td>5) 고감정지혈증, 고혈압혈증</td>
<td></td>
</tr>
<tr>
<td>6) 경구 턱선혈주에 반응하지 않는 대사소실증</td>
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</tbody>
</table>

CRC/ESRD guidelines

Adequate dialysis

- Solute clearance
  - Uremic Toxins
  - Electrolytes Regulation
  - Acid-base Balance
  - Ca-P control
- Volume homeostasis
  - Fluid Overload
  - BP control

Convensional HD
Peritoneal dialysis
On-line Hemodialfiltration
Intensive HD

An adequately treated dialysis patient is physically active, well nourished, euvoicmic and normotensive, with a maintained good quality of life and a life expectancy that is not inferior to that of healthy patients.

Cardiovascular morbidity
Adequate dialysis

- Uremic toxin removal: small-middle molecule
- Phosphate removal

Avoid intradialytic hypotension
- \( UF < 10\text{mL/hr} \)

Avoid sudden cardiac death

Table 1: Summary of Procedures and Techniques to Reduce Risk of Sudden Cardiac Death in the Hemodialysis Population

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Dialyzer selection for potassium and calcium</td>
<td>Bipper et al.</td>
</tr>
<tr>
<td>2. Monitor and adjust potassium levels at least monthly for each patient, consider panel of care, changes in meal sodium intake, or a more regular diet</td>
<td>Bipper et al.</td>
</tr>
<tr>
<td>3. Diuretics to reduce extracellular fluid volume.</td>
<td>Bipper et al.</td>
</tr>
<tr>
<td>4. Minimize the use of potassium binders.</td>
<td>Bipper et al.</td>
</tr>
<tr>
<td>5. Avoid the use of caloric dense, low-phosphate, high-sodium foods.</td>
<td>Bipper et al.</td>
</tr>
<tr>
<td>6. Avoid the use of sodium bicarbonate.</td>
<td>Bipper et al.</td>
</tr>
<tr>
<td>7. Avoid the use of sodium bicarbonate.</td>
<td>Bipper et al.</td>
</tr>
<tr>
<td>8. Avoid the use of sodium bicarbonate.</td>
<td>Bipper et al.</td>
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<tr>
<td>9. Avoid the use of sodium bicarbonate.</td>
<td>Bipper et al.</td>
</tr>
<tr>
<td>10. Avoid the use of sodium bicarbonate.</td>
<td>Bipper et al.</td>
</tr>
</tbody>
</table>

Note: These recommendations are based on observational data.


Adequate dialysis

- Residual renal function

- Preservation of RRF: important aspect of HD, PD adequacy
  - Increases clearances of middle molecule and protein bound toxins
  - Reduces inter-dialytic weight gains
  - Increases blood pressure control
  - Reduces inflammatory markers
  - Is associated with better nutrition status
  - Is associated with better quality of life

- Must try to preserve it! & Measure it!
Adequate dialysis

- Kt/Vurea Small molecule clearance
- Phosphate control
- Kt/V B,j,MG Middle molecule clearance
- Controlled fluid removal
- Preserved residual renal function
- BP control

REVIEW

The Use of a Multidimensional Measure of Dialysis Adequacy—Moving beyond Small Solute Kinetics

- Multidimensional Assessment Of Optimal Dialysis: Potential Measures
- Potential Dialytic Strategies To Achieve
  - Treatment Duration
  - Treatment Frequency
  - Incremental Dialysis
  - Preservation of Residual Kidney Function
  - Consideration of Home Dialysis
- Goals of ESRD Care
  - Maximize Quality of Life
  - Maximize Survival

Take home messages

- Adequate dialysis; improved QoL and survival rate in dialysis patient
- In HD: Minimum spKt/V > 1.2, URR > 65% per session
- In PD: total weekly Kt/V urea > 1.7
- Adequacy of dialysis should be interpreted clinically rather than by targeting only solute and fluid removal
  - Preserve residual renal function
  - Well controlled electrolyte balance, phosphate, BP (normotension), fluid balance (euvolemia)
  - Maximum small & middle molecule clearance

→ Multidimensional measure of dialysis for optimal dialysis