Hemodialysis Adequacy and Monitoring

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Outline

- Review the distribution of urea during and after a dialysis treatment
- Discuss various methods of quantifying urea clearance during hemodialysis
- Provide equations to establish and refine the initial hemodialysis prescription
- Provide examples of maintenance hemodialysis adequacy measurement
Why Is Adequacy Measurement Important?

• We are responsible for the **dose** of dialysis prescribed
  - We don’t prescribe a “whiff” of a dose of an ESA or a “smidgeon” of tacrolimus

• Less than adequate dialysis (clearance and nutrition) may be associated with poor outcomes

• You and your program will be expected to assess adequacy and reimbursement may be based on your performance
So blame some of your colleagues named:

- Warady
- Brewer
- Neu
- Goldstein
Urea Distribution: Single-Pool Model

• Urea distributed evenly across patient total body water.
• Urea removed at equivalent rates from all compartments of patient total body water:
  – Intracellular fluid
  – Extracellular fluid
    • Interstitial space
    • Intravascular space
Urea Clearance During Hemodialysis: Single-Pool Model

Hypothetical flow diagram:
- **G**: Urea Generation
- **V**: Patient Compartment
- **C**: Urea Removal
- **K*C**: Total Clearance

The diagram illustrates the process of urea clearance during hemodialysis, emphasizing the movement and clearance of urea within the patient's body.
Initial Hemodialysis Prescription: Concepts

- Aim to prescribe a dose of dialysis to effect a desired quantity of urea removal.
- Urea removal occurs by 1st order (logarithmic) kinetics.
- Initial patient Vd of urea (total body water) is unknown.
Initial Hemodialysis Prescription:

Equation

\[ \frac{Kt}{V} \sim -\ln \left( \frac{C_1}{C_0} \right) \]

- **K**: dialyzer urea clearance (ml/min)
- **t**: treatment time (minutes)
- **V**: estimated total body water (600 ml/kg)
- **C0**: predialysis BUN (mg/dl)
- **C1**: post dialysis BUN (mg/dl)
Initial Hemodialysis Prescription & Refinement: Iterative Process

\[ \text{Kt/V} \sim -\ln (C1/C0) \]

(1) Determine desired urea removal (e.g., 50%)
(2) Choose appropriate dialyzer size and enter K
(3) Estimate V (600 ml/kg)
(4) Obtain pre dialysis [BUN] C0, perform dialysis for prescribed t, obtain post dialysis [BUN] C1
(5) Calculate V using K, t, and measured C0 & C1
(6) Repeat steps 1-5 using calculated V
Initial Hemodialysis Prescription & Refinement: Example

13 year-old female with FSGS to initiate hemodialysis. Desired urea clearance is 50%.
A dialyzer with surface area 1.3m$^2$ is chosen. 
\( K_{\text{urea}} = 210 \text{ ml/min @ Qb of 250 ml/min} \)
Patient pre-dialysis weight is 42 kg.

Using equation: \( \text{Kt/V} \sim -\ln \left( \frac{C_1}{C_0} \right) \)

\[
210 \text{ ml/min} \times \frac{t}{(42\text{kg} \times 600\text{ml/kg})} = -\ln\left(\frac{50}{100}\right)
\]

leading to \( t = 83 \text{ minutes} \)
Hemodialysis performed.
Pre-HD [BUN] C₀ = 94 mg/dl
Post-HD [BUN] C₁ = 65 mg/dl
Time delivered = 83 minutes

Using equation: \( \frac{Kt}{V} \sim -\ln \left( \frac{C₁}{C₀} \right) \)

\[ 210 \text{ml/min} \times 83 \text{min} \div V = -\ln \left( \frac{65}{94} \right) \]

leading to \( V = 47.2 \text{ liters} \).
Hemodialysis Adequacy Monitoring: Moving from Initiation to Maintenance

- Initiation equation does not account for ultrafiltration—more precise equations needed
- Target weight usually determined within one month after hemodialysis initiation
- Vascular access often changes in first two months
- Hemodialysis adequacy must be measured monthly
Hemodialysis Adequacy: Urea Clearance Measurement

- Urea Reduction ratio (URR)
- Formal Urea Kinetic Modeling (UKM)
  - Single-pool Kt/V (spKt/V)
- Algebraic spKt/V Approximation
  - Daugirdas equation
- Equilibrated Double-pool Kt/V (eqKt/V)
BUN Levels and Adequacy Measurement in ESRD

Dialysis (URR, Kt/V)

Protein intake (nPCR)

Monday

Wednesday
Hemodialysis Adequacy: Urea Reduction Ratio (URR)

- \((C_0 - C_1)/C_0 \times 100\%\)
- Extremely simple to use
- Imprecise as URR does not take urea removed by ultrafiltration into account
  - A patient with a URR of 65% may have spKt/V ranging from 1.1 to 1.35 based on UF volume
- Gives no information regarding nutrition status (nPCR)
UKM Fundamentals

- UKM uses advanced computational software to solve for two factors:
  - $V_t = \text{end-dialysis urea distribution volume}$
  - $G = \text{interdialytic urea generation rate}$
- $Kt/V$ is calculated from $K_d$ (dialyzer urea clearance), $t$ (time of dialysis in minutes) and $V_t$
- $nPCR$ is calculated from $G$
UKM Fundamentals

- $V_t$ initially estimated with a formula based on height and postdialysis weight
- A computational algorithm solves for $V_t$ and $G$ by reiteration to arrive at unique values
Natural Logarithmic Kt/V Estimation

• The natural logarithm formula of Daugirdas
  – has been validated\textsuperscript{1} in children.
  – has gained acceptance\textsuperscript{1,2,3} as an accurate estimation of single-pool Kt/V in adults and children.
  – is accurate by accounting for intradialytic urea generation and removal via ultrafiltration.
  – gives no information regarding nPCR.

3. CMS-TEP, NQF
Daugirdas’ Approximation Formula

\[ \text{Kt/V} = -\ln \left( \frac{C_1}{C_0} \right) - 0.008*t + (4 - 3.5 \times \frac{C_1}{C_0}) \times \frac{\text{UF}}{W} \]

- **C_0** = predialysis BUN (mg/dl)
- **C_1** = post dialysis BUN (mg/dl)
- **t** = time on dialysis (hours)
- **UF** = ultrafiltration volume (liters)
- **W** = postdialysis weight

Natural Logarithmic Estimates of Kt/V in the Pediatric Hemodialysis Population

Stuart L. Goldstein, MD, Jonathan M. Sorof, MD, and Eileen D. Brewer, MD

American Journal of Kidney Diseases, Vol 33, No 3 (March), 1999: pp 518-522
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nPCR Estimation for Children

• Normalized protein catabolic rate (nPCR) not calculated by spKt/V estimation formulas

• No published comparison of nPCR calculated in children by UKM and algebraic methods

• Theoretical concerns regarding nPCR estimation methods in children:
  – Widely varying size among pediatric patients
  – Relatively higher protein intake (g/kg/d) prescribed for younger children
BUN Levels for nPCR

Dialysis

(C1, V1)

(C2, V2)
nPCR Estimation ($n\text{PCR}_{\text{est}}$) for Children

- Urea generation rate ($\text{estG}$, mg/min) calculated from the BUN rise between HD treatments

\[
\text{estG} = \frac{[(C2 \times V2) - (C1 \times V1)]}{t}
\]

- $n\text{PCR}_{\text{est}}$ (grams/kg/day) calculated using the modified Borah equation:

\[
\text{nPCR}_{\text{est}} = 5.42 \times \frac{\text{estG}}{V1} + 0.17
\]

Hemodialysis Adequacy nPCR Estimation

Goldstein SL: *Adv Ren Replace Ther* 2001 8:173-9

The Center for Acute Care Nephrology
nPCR assessment and IDPN treatment of malnutrition in pediatric hemodialysis patients

Table 1. Nutrition and hemodialysis adequacy parameters before and during intradialytic parenteral nutrition (IDPN) (BMI body mass index, nPCR normalized protein catabolic rate)\textsuperscript{a}

<table>
<thead>
<tr>
<th></th>
<th>Pre IDPN</th>
<th>IDPN</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Weight change</td>
<td>-0.6±2.70</td>
<td>1.8±2.1</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>% BMI change</td>
<td>-1.3±2.7</td>
<td>1.3±2.1</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>nPCR (g/kg per day)</td>
<td>1.05±0.36</td>
<td>1.35±0.37</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Serum albumin (g/dl)</td>
<td>3.7±0.8</td>
<td>3.8±0.6</td>
<td>NS</td>
</tr>
<tr>
<td>spKt/V</td>
<td>1.49±0.29</td>
<td>1.43±0.18</td>
<td>NS</td>
</tr>
</tbody>
</table>

\textsuperscript{a} All values mean monthly±SD
Normalized Protein Catabolic Rate Versus Serum Albumin as a Nutrition Status Marker in Pediatric Patients Receiving Hemodialysis

Marisa Juarez-Congelosi, RD, LD,* Pamela Orellana, RD, LD,* and Stuart L. Goldstein, MD†

Table 1. Adequacy, Normalized Protein Catabolic Rate, and Serum Albumin by Age Group

<table>
<thead>
<tr>
<th></th>
<th>INF</th>
<th>CH</th>
<th>AD</th>
<th>All</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>nPCR</td>
<td>1.63 ± 0.73</td>
<td>1.29 ± 0.33</td>
<td>1.13 ± 0.28</td>
<td>1.20 ± 0.34</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>sAlb</td>
<td>4.4 ± 0.4</td>
<td>4.1 ± 0.5</td>
<td>4.2 ± 0.4</td>
<td>4.2 ± 0.5</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>spKt/V</td>
<td>1.94 ± 0.42</td>
<td>1.53 ± 0.22</td>
<td>1.43 ± 0.15</td>
<td>1.48 ± 0.21</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>eqKt/V</td>
<td>1.74 ± 0.38</td>
<td>1.33 ± 0.33</td>
<td>1.24 ± 0.17</td>
<td>1.27 ± 0.19</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

nPCR, normalized protein catabolic rate; sAlb, serum albumin; spKt/V, single-pool Kt/V; eqKt/V, estimated equilibrated Kt/V; INF, infant; CH, child; AD, adolescent.

*Analysis of variance comparing mean values (± standard deviation) across age strata.
Weight loss: 2% monthly weight loss for 3 consecutive months
Case #1: Real Weight Gain

- Patient with increasing weight, adequate nutrition (nPCR) and decreasing spKt/V
- Recommend increase of dialyzer size or time of treatment

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>SpKt/V</th>
<th>nPCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>34.3</td>
<td>1.40</td>
<td>1.20</td>
</tr>
<tr>
<td>35.2</td>
<td>1.32</td>
<td>1.15</td>
</tr>
<tr>
<td>36.1</td>
<td>1.21</td>
<td>1.18</td>
</tr>
</tbody>
</table>
Case #2: Fluid Weight Gain

- Patient with increasing weight, decreasing spKt/V and worsening nPCR
- Check for edema, hypertension, albumin level
- Recommend decreasing target weight, addressing nutrition

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>SpKt/V</th>
<th>nPCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>34.3</td>
<td>1.40</td>
<td>1.20</td>
</tr>
<tr>
<td>35.2</td>
<td>1.32</td>
<td>0.89</td>
</tr>
<tr>
<td>36.1</td>
<td>1.21</td>
<td>0.65</td>
</tr>
</tbody>
</table>
Case #3: Catabolic State

- Patient with decreasing weight, stable Kt/V and rising nPCR
- Severe malnutrition
- Recommend aggressive nutrition management

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>SpKt/V</th>
<th>nPCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>34.3</td>
<td>1.40</td>
<td>1.20</td>
</tr>
<tr>
<td>32.5</td>
<td>1.32</td>
<td>1.65</td>
</tr>
<tr>
<td>31.6</td>
<td>1.35</td>
<td>1.7</td>
</tr>
</tbody>
</table>
Urea Distribution: Double-Pool Model

- Urea is distributed evenly prior to dialysis.
- Urea removed from intravascular space during hemodialysis.
- A urea concentration disequilibrium is created between the ICF and ECF during hemodialysis.
Urea Rebound after Hemodialysis

[BUN]

End of Dialysis

The Center for Acute Care Nephrology
Equilibrated Kt/V Estimation Methods

- **Rate equation (Daugirdas)\(^1\)**
  - Used in HEMO Study
  - Arterial \(\text{eqKt/V} = \text{spKt/V}(1-0.6/t_{\text{hours}}) + 0.03\)
  - Venous \(\text{eqKt/V} = \text{spKt/V}(1-0.4/t_{\text{hours}}) + 0.02\)

- **Mid-Dialysis Method (Smye)\(^2\)**

- **Log Extrapolation of 15 min post-HD BUN (Goldstein)\(^3\)**
  - Estimate of \(\text{eqBUN}\) extremely accurate

- **Linear regression model (Marsenic)\(^4\)**
  - \(C_{eq} (\text{mmol/L}) = 1.085 \times Ct + 0.729\)

Urea Rebound after Hemodialysis

\[ \text{eqBUN} = \text{BUN}_{30\text{sec}} + (\text{BUN}_{15\text{min}} - \text{BUN}_{30\text{sec}})/0.69 \]
## Equilibrated Kt/V Estimation Methods: Pediatric Study

<table>
<thead>
<tr>
<th>Method</th>
<th>Total % error</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Daugirdas (Rate equation)</strong></td>
<td>11.3% to 25.6%(^1,2)</td>
</tr>
<tr>
<td><strong>Smye (Mid-Dialysis)</strong></td>
<td>46%(^1)</td>
</tr>
<tr>
<td><strong>Goldstein (Log extrapolation)</strong></td>
<td>8%(^2)</td>
</tr>
<tr>
<td><strong>Marsenic (Linear Regression)</strong></td>
<td>26.5%(^3)</td>
</tr>
</tbody>
</table>

Comparison of single-pool and equilibrated Kt/V values for pediatric hemodialysis prescription management: analysis from the Centers for Medicare & Medicaid Services Clinical Performance Measures Project

- Do we really need eKt/V to manage patients month-to-month?
- CMS’ CPM project assessed pediatric HD patient spKt/V and eKt/V to ascertain if results would lead to management differences
- \([\text{spKt/V} - \text{eKt/V}] > 0.20\) used as threshold
Comparison of single-pool and equilibrated Kt/V values for pediatric hemodialysis prescription management: analysis from the Centers for Medicare & Medicaid Services Clinical Performance Measures Project

- Very low discordance rates between spKt/V and eKt/V near K-DOQI target
- Discordance rate increased at higher Kt/V values

<table>
<thead>
<tr>
<th>Adequacy cutoff</th>
<th>AV (n=720)</th>
<th>VV (n=793)</th>
<th>Discordance rate(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. spKt/V &gt;1.2 and estimated eKt/V &lt;1.0</td>
<td>3</td>
<td>2</td>
<td>0.3%</td>
</tr>
<tr>
<td>2. spKt/V &gt;1.4 and estimated eKt/V &lt;1.2*</td>
<td>24</td>
<td>2</td>
<td>1.7%</td>
</tr>
<tr>
<td>3. spKt/V &gt;1.6 and estimated eKt/V &lt;1.4*</td>
<td>63</td>
<td>20</td>
<td>5.5%</td>
</tr>
</tbody>
</table>

\(^a\)Discordance rate = number of discordant values/1,513 samples
*p<0.05 comparing row 2 or row 3 with row 1
Two-point normalized protein catabolic rate overestimates nPCR in pediatric hemodialysis patients

Poyyapakkam R. Srivaths • Scott Sutherland • Steven Alexander • Stuart L. Goldstein

Table 2 Comparison of BUN and nPCR

<table>
<thead>
<tr>
<th>Total patient sample cohort (n=76)</th>
<th>Percent of samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two-point model incorrectly categorizes nPCR as &gt;1</td>
<td>7</td>
</tr>
<tr>
<td>Two-point model incorrectly categorizes nPCR as &lt;1</td>
<td>1</td>
</tr>
<tr>
<td>Two-point and three-point nPCR calculations agree</td>
<td>68</td>
</tr>
</tbody>
</table>

Table 3 Difference between two-point and three-point nPCR results

Values expn BUN blood normalize p

\( p \) value

\( =0.0001 \)

\( =0.0000 \)
Frequent HD Dose Calculation

• How do we convert from 3x weekly hemodialysis to more frequent hemodialysis?
• Simply algebra is not accurate
• Standard Kt/V (stdKt/V)
Rationale for stdKt/V

• Therapies that achieve the same mean pre-treatment BUN concentrations are equivalent in delivered dose and should produce similar patient outcomes
• Should be based on eKt/V
stdKt/V calculation

\[ e^{Kt/V} = 0.924 \times spKt/V - 0.395 \times spKt/V/t + 0.056 \]  \hspace{1cm} (4)

\[ stdKt/V = 168 \times (1 - \exp[-Kt/V])/t/[(1 - \exp[-Kt/V])/(Kt/V) + 168/(N \times t) - 1] \]  \hspace{1cm} (3)

1. \( spKt/V \) calculated using Daugirdas II
2. \( t = \) treatment time in hours
3. \( Kt/V \) in stdKt/V calculation is \( eKt/V \)

Fig. 2. Calculated values of urea e\(Kt/V\) calculated using equation 4 compared with those directly measured.
stdKt/V ≥ 2.0 was best (93.5% sensitivity/96.7 % specificity) to predict spKt/V > 1.2

stdKt/V ≥ 2.2 was best (73.4% sensitivity/96.1 % specificity) to predict spKt/V > 1.4
Conclusions

HD Adequacy measurement via Kt/V and nPCR is an essential and required component of hemodialysis care delivery.

Understanding adequacy variables can improve patient care.

HD adequacy calculations are not complex.

Email me for XLS spreadsheets

stuart.goldstein@cchmc.org