PERITONEAL DIALYSIS ADEQUACY: The KDOQI Guidelines and Beyond

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Disclosure of Financial Relationships

John M. Burkart, MD

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08/14

LECTURE OUTLINE

Adequacy of PD

• General comments on “adequacy” measurements
• PRCTs used to develop Guidelines / Targets
• Comparison with HD
• Remember there are other solutes
• Importance of RKF

ADEQUATE DIALYSIS BY CLINICAL CRITERIA

• Absence of uremic symptoms
• Optimization of well-being
• Normal nutrition and its consequences
• Normal volume homeostasis and its consequences
• Rehabilitation to best potential
• Consider including the following: Normalization of all functions of the native kidneys
  – Includes more than just solutes and water removal

PROBLEMS IN ONLY USING CLINICAL CRITERIA FOR DETERMINING “ADEQUACY”

• Confounding co-morbid disease
  – Gastropareisis
  – CHF
• Patients often minimize symptoms because they do not want to do more.
• By time of clinical recognition, is it “too late?”
• Lab measures can be misleading
  – High creatinine may be due to large muscle mass = good
  – High BUN may reflect high protein intake but OK dialysis.
  – But either could be high due to underdialysis = bad

Ideal Marker of Dialysis Adequacy

• Retained in renal failure
• Eliminated by dialysis
• Easily measured
• Proven dose-related toxicity
• Generation and elimination representative of other toxins of similar molecular weight

PROBLEM: what about various molecular weight toxins?
• I.e. MMW solutes vs. SMW solutes (B12 vs Urea)

Adapted from Vanholder
ADEQUACY OF DIALYSIS

- We have historically used small solute removal as a surrogate for adequacy.
  - Urea based ([urea], TAC, Clearance, URR, Kt/V urea)
  - Symptoms are related to these
  - The concentration of Urea is generally markedly higher than other solutes
  - Easy to measure

ASSUMING WE USE A LABORATORY SURROGATE, WHAT SURROGATE SHOULD WE USE AS AN ADEQUACY METRIC?

How do we best quantify the removal of the solute in question from body
  - GFR
  - Creatinine Clearance
  - Litters process / min or day
  - Kt/V?

Does it matter what we normalize to?
  - Kt/V or KT/BSA
  - Secondary analysis of Hemo Trial data gender and V vs BSA

Does it matter what metric we use based on the solute in question?
  - Small solute, Middle molecules, Etc.
  - Kt/V urea, Kt/V β2microglobulin, etc.

IS A PERSON IN NORMAL HEALTH WELL DIALYZED BY OUR CURRENT STANDARDS?

- What is your Kt/V urea?
- What is your URR?

WHAT IS YOUR Kt/V or URR?

- Kt/V urea
  - About 25 - 26/week
    - Assumes 100 ml/min urea clearance (K)
    - 10,080 minutes in a week (t)
    - A volume of distribution of 40 liters (V)
- URR
  - About zero!
    - Similar to URR in PD

ACKNOWLEDGED THAT UREMIA NOT UREA ONLY!

- PD vs CHD clinical outcomes similar despite differences in Kt/V
- What about PO₄, Middle Molecules, Protein bound Solutes, etc.?
- Residual Syndrome in long term patient despite history of “Adequate Dialysis” in terms of Kt/V urea.

Some organic compounds that accumulate in uremia (Bergstrom, Van Holder)

- Urea
- Creatinine
- Guanidines
- Uric acid
- Pyridine compounds
- Aliphatic amines
- Aromatic amines (protein bound)
- Indoles
- Phenols
- Hippurates
- Myoinositol
- Glucuronic acid
- Oxalic acid
- Advanced glycosylation end products
- Furan carboxylic acids
UREMIC TOXINS

Small Molecular Weight Toxins
- MW 60 to 500 Daltons
  - Urea, Creatinine easily removed by diffusion

Middle Molecular Weight Toxins
- MW > 500 Da
  - β2-Microglobulin is prototype
  - Most are peptides, difficult to remove unless membrane pore size is large
  - Convection very helpful

Protein Bound Toxins
- P-cresylsulfate is prototype
- Protein bound (mainly albumin)
  - Difficult to remove no matter what type of dialysis

Beta2-Microglobulin
- Surrogate or prototype middle molecule
- MW 11,800 Da
- Part of major histocompatibility locus
- Generation rate fairly constant
  - Not related to cardiac damage such as proBNP or ANP
- Filtered by Glomeruli
- Reabsorbed & degraded in proximal convoluted tubules
- In health renal catabolism about 150 to 220 mg/d
- Plays a role in dialysis acquired amyloidosis

PROTEIN BOUND SOLUTES RETAINED IN UREMIA

- Most are produced by gut.
- Production rates vary widely.
- Levels correlate with outcome.
- Lower levels in PD patients.
- HD may remove these solutes by diffusion or convection more efficiently than PD. However PD has more albumin loss than HD (and therefore also these bound solutes).
- Elimination of these solutes is more dependent on residual function than that for urea.

WAYS TO QUANTIFY SMALL SOLUTE REMOVAL (Kd)

- Measure clearance: using appropriate collections and Lab data with subsequent calculation.
  - HD – Collect all spend dialysate and urine with appropriate blood, urine and dialysate samples
  - PD – 24 hour collection of dialysate and urine with appropriate blood, urine and dialysate samples
- Estimate using a Mathematical model:
  - HD – URR or Kt/V from Blood samples
  - PD – Estimated from PET data, 24 hour collection of urine

CURRENTLY USED SURROGATE FOR SMALL SOLUTRE CLEARANCE:

\[ Kt/V_{urea} \]

\[ Kt/V = Kd \text{ (ml/min)} \times T \text{ (min)} / V \text{ (ml)} \]

Where:
- Kd is clearance of the dialysis system or “Dialyzer”
- T = time
- V = volume of distribution of solute (urea) in question

REMOVAL AMOUNT IN PD

\[ \text{Removal} = \text{total DV} \times \text{[concentration]} \]
CLEARANCE (K) IN PD – Kt/V

- \( K = \frac{UV}{P} = \text{Drain Volume (DV)} \times \text{D/P concentration) / unit time} \)
- \( T = \text{time – classically is a day} \)
- \( V_{\text{urea}} = \text{volume of distribution} \)

\[
K = \text{totalDV} \times \text{D/P ratio} \\
Kt/V = \frac{\text{Total DV} \times \text{D/P ratio}}{V_{\text{urea}}} \\
\]

ARS QUESTION #1

Mr. Smith is an anuric 92 Kg male (Body water = 50 liters) who is on CAPD. He does four 2.5 liter exchanges/day. His total effluent Drain volume is 12 L. His serum Urea is 12 and his dialysate urea is 10.8.

What is his daily Kt/V?
1. 0.289
2. 0.216
3. 1.75
4. 0.241

ARS QUESTION #2

Mr. Smith is an anuric 92 Kg male (Body water = 50 liters) who is on CAPD. If his drain volumes are 90% saturated with urea (D/P ratio for urea = 0.9)

Which of the following treatments below would give him a weekly Kt/Vurea of > 1.7?
1. Five 2.5 liter dwells (12.5 L total) and 2 liters of UF/day
2. Four 3 liter dwells and 1 liter of UF/day
3. Five 2 liter dwells and 3 liters of UF/day
4. Five 2 liter dwells and 2 liters of UF/day

Kt/Vurea CALCULATION IN PD

\[
Kt/V_{\text{urea}} = \frac{\text{Total Drain Volume} \times \text{D/P}_{\text{urea}}}{\text{Volume Distribution}_{\text{urea}}} \\
\]

So if a patient is anuric and in a day -
10 liters instilled and UF of 2 liters, drain volume = 12L
The equilibration / exchange is 90% then D/P = 0.9
The Volume Distribution_{urea} is 40 than V = 40

Then –
\[
Kt/V_{\text{urea}} \text{ / day} = 10 \times 0.9/40 = 0.225 \\
0.225 / \text{day} \times 7 \text{days/week} = 1.575 / \text{week} \\
\]

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**KT/V$_{urea}$ and PD – Key Take Home Points**

- Target minimal total (RKF and PD) weekly KT/V$_{urea}$ in PD is:
  - $KT/V_{urea} > 1.7 / \text{week}$.
- If anuric: minimal PD $KT/V_{urea}/\text{day}$ should be:
  - $> 0.25/\text{day}$
  - $7 \times 0.035 = 1.75$
- Therefore you at least need a 100% saturated DV/day of at least 25% of patients body water or V
  - daily $KT/V_{urea} = \text{Saturated DV/V} = 0.25$

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1. Five 2.5 liter dwells (12.5 L total) and 2 liters of UF/day
   - $14.5 \times 0.9 = 13.05$
2. Four 3 liter dwells and 1 Liter of UF/day
   - $13 \times 0.9 = 11.7$
3. Five 2 liter dwells and 3 liters of UF/day
   - $13 \times 0.9 = 11.7$
4. Five 2 Liter dwells and 2 liters of UF/day
   - $12 \times 0.9 = 10.8$

**LECTURE OUTLINE**

*Adequacy of PD*

- General comments on “adequacy” measurements
- PRCTs used to develop Guidelines / Targets
- Comparison with HD
- Remember there are other solutes
- Importance of RKF

**For PD: The Original Publication!**

Adequacy of Dialysis and Nutrition in Continuous Peritoneal Dialysis: Association with Clinical Outcomes

CARAGALDA (CARAGA) Peritoneal Dialysis Study Group$^{1,2}$

JASN 7:198, 1996

**RELATIONSHIP BETWEEN DIALYSIS KT/V$_{urea}$ and PROBABILITY OF FAILURE**

Probability of failure – Is it a step function?

Gotch & Sargent Ki 29:529, 1985
ADEQUACY of PD ARS #3

A 60 year old female with ESRD from DM is on CAPD. Her Kt/V is barely above goal and she is overall doing well. Her D/P creat on a 4 hour 2.5% Dextrose PET is 0.54

She wants to change to APD with a LBF and no mid day exchange

If she does, which one of the following would likely be true?

1) If similar infused volume used, Her PO4 and Creat removal would likely significantly decrease despite minimal change in Kt/V
2) She would need less overall dialysate to maintain all target clearances
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POSSIBLE CLINICAL RAMIFICATIONS OF RETAINED MMW SOLUTES IN UREMIA

Probably related to some of the long term complications of uremia
- Dialysis acquired amyloidosis
- Accelerated CV risk profile
- Uremic platelet dysfunction
- Immunodeficiency
**Hemodialysis (HEMO) Study: Treatment Characteristics**

<table>
<thead>
<tr>
<th>Treatment Variable</th>
<th>Standard-Dose</th>
<th>Max-Dose (N=290)</th>
<th>Low-Flux (N=230)</th>
<th>Max-Flux (N=270)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of dialysis session (min)</td>
<td>196±20</td>
<td>219±23</td>
<td>266±28</td>
<td>20±27</td>
</tr>
<tr>
<td>Rate of blood flow (mL/min)</td>
<td>311±51</td>
<td>375±32</td>
<td>344±53</td>
<td>361±54</td>
</tr>
<tr>
<td>Rate of ultrafiltrate (mL/min)</td>
<td>298±25</td>
<td>351±18</td>
<td>33±27</td>
<td>25±28</td>
</tr>
<tr>
<td>Total volume changes/90 min (L)</td>
<td>59±7.6</td>
<td>55±2.7</td>
<td>65±19.3</td>
<td>62±2.9</td>
</tr>
<tr>
<td>Age (y)</td>
<td>62±10.9</td>
<td>62±11.4</td>
<td>62±11.5</td>
<td>62±11.5</td>
</tr>
<tr>
<td>Diabetes</td>
<td>18%</td>
<td>20%</td>
<td>19%</td>
<td>18%</td>
</tr>
<tr>
<td>Serum albumin (g/dL)</td>
<td>4.0±0.6</td>
<td>4.0±0.6</td>
<td>4.0±0.6</td>
<td>4.0±0.6</td>
</tr>
<tr>
<td>Blood urea nitrogen (mg/dL)</td>
<td>62±13.6</td>
<td>66±14.8</td>
<td>55±15.5</td>
<td>57±13.1</td>
</tr>
</tbody>
</table>

**HEMO Study – Primary Outcome Data: Survival by Dose & Flux**

![Graph showing survival by dose and flux](Eknoyan et al., NEJM 2002)

**Hemo Study: Relative Risk Analysis – Entire Cohort**

![Graph showing relative risk analysis](Eknoyan et al., NEJM 2002)

**Predictors of Cardiac Mortality in HEMO Trial**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative mean potassium levels at 1 year during follow-up (per 1 mg/dl increase)</td>
<td>1.30 (1.09 to 1.53)</td>
<td>0.007</td>
</tr>
<tr>
<td>Age (per 10 years increase)</td>
<td>1.35 (1.05 to 1.74)</td>
<td>0.016</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>1.50 (1.05 to 2.15)</td>
<td>0.026</td>
</tr>
<tr>
<td>Race (black)</td>
<td>1.75 (1.37 to 2.24)</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.68 (1.30 to 2.17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albuminuria (per 1 g/L increase)</td>
<td>1.35 (1.05 to 1.74)</td>
<td>0.016</td>
</tr>
<tr>
<td>Residual fractional sodium clearance (per 1%/min increase)</td>
<td>1.05 (0.95 to 1.16)</td>
<td>0.306</td>
</tr>
<tr>
<td>High flux dialysis</td>
<td>1.39 (0.91 to 2.12)</td>
<td>0.166</td>
</tr>
</tbody>
</table>

**Free Serum p-Cresol Levels Predict Survival in HD**

![Graph showing free serum p-cresol levels](Bammens et al, 2006; KI 69:1081-1087)

**European Best Practice Guidelines**

- Recommend using B2M as a surrogate for MMW solutes
- Recommend Maximizing its removal.
In original analysis of data:
• Every 1 mg/L increase in B2M was associated with a 2% increase in RR of death
• *****Was not corrected for effect of RKF

**EFFECT OF ON-LINE HEMODIAFILTRATION ON ALL CAUSE CV MORTALITY**

The Convective Transport Study (CONTRAST)
- Randomized 714 chronic HD patients
  - 356 to on-line post-dilution hemodiafiltration
  - 358 to standard low flux dialysis
- Results:
  - For entire group no difference in all cause mortality between hemodiafiltration and standard low flux HD
  - High Volume hemodiafiltration (>22L of replacement fluids) was associated with a survival advantage

**REPORTS FROM THREE RCTs**

**HDF vs HD**

- Turkish study (Ok et al, NDT 28:192, 2013) —
  - No benefit
- CONTRAST study (Grooteman et al, JASN 23:1087, 2012) —
  - No benefit
- ESHOL (Mauzel et al, JASN 24: 2013) —
  - marked benefit (30% lower all cause mortality)

Benefits of HDF vs. HD remain controversial
• ? Better survival with larger convective volumes?.

**IMPORTANCE OF 24 HOURS/DAY PD DWELL FOR MMW SOLUTES**

• Compared 2 exchanges over 12 hours to 2 exchanges over 24 hours (dextrose)
• Found similar SMW but markedly different MMW clearances

**Dissociation between Clearance of Small and Middle Molecular Weight Toxins**

- As you increase # exchanges/24 hours SMW clearance improves
- As you increase # exchanges/24 hours MMW clearance does NOT improve

**Kim et al, PDI 2001; 21:462-466**

**Kim et al, ND & T 21;2001**
THREE PORE MODEL:
Fractional Amount of Total Pore Area

- Large Pores (100-200 A)
  - About 2% of total
- Small Pores (40-60 A)
  - About 95% of total
- Ultrapores (4-6 A)
  - About 3% of total

Dextrose vs. Icodextrin Net UF
THEORETICAL CONSTRUCTS

\[
\begin{array}{cccc}
\text{Time (hr)} & \text{0} & \text{2} & \text{4} & \text{6} & \text{8} & \text{10} & \text{12} & \text{14} & \text{16} \\
\text{Net UF (ml)} & -800 & -600 & -400 & -200 & 0 & 200 & 400 & 600 & 800 & 1000 & 1200 \\
\hline
\text{2.5% Dex.} & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet \\
\text{4.25% Dex.} & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet \\
\text{7.5% Icodex} & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet \\
\end{array}
\]

Ho-Dac-Pannekeet et al, Kid Int 1996; 50:979-86
Douma et al, Kid Int 1998; 53:1014-21

THEORETICAL CONSTRUCTS
FOR
POTENTIAL UF VOLUMES
DEXTROSE DWELL

\[
\begin{array}{cccc}
\text{Time (hours)} & \text{0} & \text{0.2} & \text{0.4} & \text{0.6} & \text{0.8} & \text{1.0} & \text{1.2} & \text{1.4} & \text{1.6} & \text{1.8} & \text{2.0} \\
\text{Urea} & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet \\
\text{Creatinine} & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet \\
\text{β2-Microglobulin Clearance} & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet & \bullet \\
\end{array}
\]

\[P = .008, \text{ icodextrin vs 1.5% dextrose, } P = .01, \text{ icodextrin vs 4.25% dextrose.}\]

Suggests
\[
\begin{array}{cccc}
\text{β2 Clearance is:} & \text{a) UF related} & \text{b) Icodextrin UF is} & \text{via small pores,} & \text{Dextrose via} & \text{both aquaporins and small pores} \\
\end{array}
\]

β2-Microglobulin Clearance
Timed 4 hour dwell -- Icodextrin vs Dextrose

MIDDLE MOLECULES

- Probably important
- 24 hours/day of PD dwell once minimal RRF
- Subgroup analysis of HEMO trial data
- But? Recent Hemodialfiltration data goes against it

PD - DIFFUSION CURVES:
Rate of Diffusion Dependent on Size

\[
\begin{array}{cccc}
\text{Dialysate to plasma (D/P) ratios} & \text{0.2} & \text{0.4} & \text{0.6} & \text{0.8} & \text{1.0} \\
\text{Dwell time (hours)} & \text{Urea} & \text{Creatinine} & \text{MM} \\
\end{array}
\]

Davis KI 2006; 70(suppl):S76

PERITONEAL EQUILIBRATION TEST

Twardowski et al PDB 1987

Based on standard 4 hour dwell with 2.5% dextrose
Can be used to classify peritoneal transport

D/P FOR SOLUTES RELATED TO DWELL TIME AND MOLECULAR WEIGHT IN PD

DIFFUSION CURVES FOR SOLUTES OF VARYING SIZE

Urea
Creatinine

Dwell time (hours)

COMPARISON of Kt/V and CCr on PD
assumes 2.5L fill, Anuria, BSA of 1.72-2.0 m²

PROFILE OF A PD PRESCRIPTION

Diffusion of urea stops in average patient
Diffusion of creatinine stops in average patient
UF stops in average patient with 1.5%D
AFFECT OF PD TRANSPORT ON CCr – NIPD PATIENTS

<table>
<thead>
<tr>
<th>Transport Category</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Transporters</td>
<td>33.7</td>
<td>39.8</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>34.3</td>
<td>40.5</td>
</tr>
<tr>
<td>Low Transporters</td>
<td>40.0</td>
<td>47.2</td>
</tr>
<tr>
<td>Mean</td>
<td>44.7</td>
<td>52.7</td>
</tr>
<tr>
<td>High average transporters</td>
<td>48.0</td>
<td>56.6</td>
</tr>
<tr>
<td>Mean + SD</td>
<td>50.8</td>
<td>59.9</td>
</tr>
<tr>
<td>High Transporters</td>
<td>55.6</td>
<td>65.6</td>
</tr>
</tbody>
</table>

Assumptions = Kt/V of 2.2, anuric, hourly 2 L exchanges V=41.7 M, 32.1 F

Twardowski JA PD 1998

PO₄ REMOVAL IS RELATED TO TRANSPORT TYPE (and Rx)

PO₄ REMOVAL BY PD
Correlation with Modality and Membrane Transport Characteristics

<table>
<thead>
<tr>
<th></th>
<th>CAPD</th>
<th>APD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peritoneal Kt/V</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>1.47 ± 0.5</td>
<td>1.09 ± 0.4</td>
</tr>
<tr>
<td>High Average</td>
<td>1.14 ± 0.51</td>
<td>1.16 ± 0.5</td>
</tr>
<tr>
<td>Low Average</td>
<td>1.06 ± 0.2</td>
<td>1.46 ± 0.4</td>
</tr>
<tr>
<td>Low</td>
<td>1.58 ± 0.3</td>
<td>1.44 ± 0.3</td>
</tr>
<tr>
<td>Peritoneal PO₄ Cl</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>46.9 ± 12.6</td>
<td>48.1 ± 13.0</td>
</tr>
<tr>
<td>High Average</td>
<td>39.3 ± 10.4</td>
<td>39.6 ± 9.3</td>
</tr>
<tr>
<td>Low Average</td>
<td>35.9 ± 7.8</td>
<td>31.6 ± 6.6</td>
</tr>
<tr>
<td>Low</td>
<td>33.9 ± 15.2</td>
<td>24.5 ± 9.0</td>
</tr>
</tbody>
</table>

Bernardo et al. CJASN 6:591-597, 2011

ADEQUACY of PD ARS #3

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She wants to change to APD with a LBF and no mid day exchange

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4) Her PO₄, Creat Cl and Kt/V would likely remain unchanged if she uses the same amount of dialysate.

HIGHLIGHTS OF 2006 PD ADEQUACY GUIDELINES

- A “minimal” recommended total solute clearance vs “Target” total solute clearance
- New total solute clearance Target — weekly Kt/Vurea of > 1.7 for all PD (CAPD and CCPD)
- Less frequent measurements
- No longer recommends monitoring/targeting creatinine clearance
- New guidelines on:
  - Initiation of Dialysis
  - Volume control
  - Protection of residual renal function
  - Quality Improvement
- Guidelines (6) and Clinical Practice Recommendations

Guideline 4. Maintenance of Euvolemia

- 4.1 Each facility should implement a program that monitors and reviews peritoneal dialysate drain volume, residual renal function and patient blood pressure on a monthly basis. Grade B
- 4.2 Some of the therapies one should consider to optimize extracellular water and blood volume include but are not limited to, restricting dietary sodium and water intake, use of diuretics in patients with residual renal function and optimization of the peritoneal ultrafiltration volume and sodium removal. Grade B
Maintenance of Euvolemia

- Facilities should have a regular process in place to review factors associated with euvolemia on a monthly basis.
- Therapies to consider to help maintain euvolemia include:
  - Restricting dietary sodium intake
  - Restricting fluid intake
  - Use of diuretics in patients with residual kidney function
  - Optimization of PD prescription

PROFILE OF A PD PRESCRIPTION

Lecture Outline

Adequacy of PD

- General comments on “adequacy” measurements
- PRCTs used to develop Guidelines / Targets
- Comparison with HD
- Remember there are other solutes
- Importance of RKF

Residual Renal Function is Predictive of LVH


Predictors of survival in ADEMEX CAPD patients; multivariate Cox regression analysis

<table>
<thead>
<tr>
<th>Factor</th>
<th>Reference</th>
<th>RR</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>per 10 y</td>
<td>1.16</td>
<td>0.007</td>
</tr>
<tr>
<td>DM</td>
<td>no DM</td>
<td>1.76</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Albumin*</td>
<td>0.1 g/dl</td>
<td>0.91</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Renal CrCl*</td>
<td>10 L/wk</td>
<td>0.89</td>
<td>0.01</td>
</tr>
<tr>
<td>pCrCl*</td>
<td>10 L/wk</td>
<td>1.03</td>
<td>0.56</td>
</tr>
</tbody>
</table>

*time dependent

Panigagua, J Am Soc Nephrol, 2002

Re-analysis of CANUSA data


Table 3. Cox model of relative risk for death with urine volume forced in as a time-dependent covariate

<table>
<thead>
<tr>
<th>Variable</th>
<th>Relative Risk</th>
<th>95% Confidence Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (1 yr older)</td>
<td>1.02</td>
<td>1.002-1.041</td>
</tr>
<tr>
<td>CVD</td>
<td>2.37</td>
<td>1.465-3.831</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.31</td>
<td>0.807-2.134</td>
</tr>
<tr>
<td>Serum albumin (1 g/L increase)</td>
<td>0.96</td>
<td>0.914-1.003</td>
</tr>
<tr>
<td>LA transport</td>
<td>1.84</td>
<td>0.418-8.075</td>
</tr>
<tr>
<td>HA transport</td>
<td>2.71</td>
<td>0.631-11.623</td>
</tr>
<tr>
<td>H transport</td>
<td>2.46</td>
<td>0.523-11.390</td>
</tr>
<tr>
<td>SGA (1 unit greater)</td>
<td>0.78</td>
<td>0.675-0.876</td>
</tr>
<tr>
<td>Urea (L/week per 1.73 m² greater)</td>
<td>0.93</td>
<td>0.795-1.079</td>
</tr>
<tr>
<td>GFR (L/week per 1.73 m² greater)</td>
<td>0.99</td>
<td>0.943-1.044</td>
</tr>
<tr>
<td>Urine volume (270 mL and daily greater)</td>
<td>0.64</td>
<td>0.506-0.890</td>
</tr>
</tbody>
</table>
Relationship between residual renal function and mortality in 1187 PD patients in the US

Renal Kt/V quartiles
1: 0.0 – 0.14
2: 0.15 – 0.40
3: 0.41 – 0.77
4: > 0.77


RKF in ADEMEX & OTHER STUDIES

Internal Consistency

All show importance of residual kidney function. Not dialysis dose!

<table>
<thead>
<tr>
<th>Factor</th>
<th>CANUSA Rel. Risk</th>
<th>Rocco et al Odds Ratio</th>
<th>ADEMEX Rel. Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 10 yr)</td>
<td>1.33 (p=0.003)</td>
<td>1.40 (p=0.01)</td>
<td>1.16 (p=0.007)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.43 (p=0.151)</td>
<td>2.40 (p=0.01)</td>
<td>1.76 (p=0.001)</td>
</tr>
<tr>
<td>pCCr (per 10L)</td>
<td>1.04 (p=0.864)</td>
<td>0.90 (p=0.41)</td>
<td>1.03 (p=0.585)</td>
</tr>
<tr>
<td>iCCr (per 10L)</td>
<td>0.83 (p=0.901)</td>
<td>0.60 (p=0.001)</td>
<td>0.89 (p=0.014)</td>
</tr>
<tr>
<td>Age (per 10 yr)</td>
<td>1.33 (p=0.002)</td>
<td>1.30 (p=0.003)</td>
<td>1.16 (p=0.007)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.38 (p=0.197)</td>
<td>1.90 (p=0.01)</td>
<td>1.77 (p=0.001)</td>
</tr>
<tr>
<td>pKt/V</td>
<td>0.88 (p=0.001)</td>
<td>0.88 (p=0.003)</td>
<td>0.94 (p=0.005)</td>
</tr>
</tbody>
</table>

PD ADEQUACY SUMMARY

Take home points

- Minimal total solute clearance goal is a total weekly Kt/V urea of > 1.7
- Know how to calculate Kt/V
- Remember the daily Kt/V should be at least 0.25 and the amount of saturated dialysate needs 25% of patients V.
- Understand differences in rate of diffusive removal based on molecular weight/size
- Transport is characterized using PET
- Middle molecule weight removal is optimized using 24 hours/day dwell
- Preserve residual renal function

For more information, see on line only lecture by Burkart on physiology

Example of CAPD prescriptions

- Standard CCPD
- CAPD with increased instilled volume overnight
- CAPD with increased # and increased overnight volumes and Nightly Exchange Device (NXD)

Example of APD prescriptions

- NIPD
- NIPD with an increased time on cycler (or manual exchange)

Thanks

Questions?
**EXAMPLE of APD PRESCRIPTIONS**

<table>
<thead>
<tr>
<th></th>
<th><strong>CCPD</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Standard CCPD</strong></td>
<td></td>
</tr>
<tr>
<td><strong>CCPD with increased instilled volume overnight</strong></td>
<td></td>
</tr>
<tr>
<td><strong>CCPD with increased # and increased overnight volumes</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Daytime</strong> (15 hours)</td>
<td></td>
</tr>
<tr>
<td><strong>night</strong> (9 hours)</td>
<td></td>
</tr>
</tbody>
</table>

**REMOVAL AMOUNT IN PD**

- Removal = [concentration] x Drain Volume (DV)

- Removal = total DV x [concentration]

**CLEARANCE (K) IN PD – Kt/V**

- $K = \frac{UV}{P} = \frac{\text{Drain Volume} (DV) \times (D/P \text{ concentration})}{\text{unit time}}$

- $T = \text{time} – \text{classically is a day}$

- $V_{\text{urea}} = \text{volume of distribution}$

- $K = \text{total DV x D/P ratio}$

- $Kt/V = \frac{\text{Total DV x D/P ratio}}{V_{\text{urea}}}$

**WHAT IS Kt/V?**

- $Kt/V = \text{fractional urea clearance}$

- $K = \text{dialysis system’s urea clearance (ml/min or L/hr)}$

- $t = \text{time on dialysis (min or hr)}$

- $V = \text{volume of distribution of urea (ml or L)}$

- $K = \frac{\text{L/hr x hr = LITRES}}{V = \text{LITRES}}$

- $Kt/V = \text{LITRES/LITRES}$

- = dimensionless ratio