Hemodialysis Adequacy

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Dialysis up-grade course

✓ Identify adequacy of dialysis and its components
✓ Learn about optimal dialysis
✓ Know dialyzers choosing by knowing which fits who and which for what
✓ Practice adequacy calculation
✓ Understand management of anemia and MBD
✓ Understand the importance of nutritional needs
✓ Understand the importance of water quality
✓ Approach HDF
Hemodialysis adequacy mission

The mission : Optimize survival, improve QoL..
The target  : Optimal dialysis
The team   : all unit staff

This mission is team work and efforts of everybody
Optimal Dialysis

- Anemia management
- BP control
- Good nutrition
- Adequate solute removal
- Fluid and electrolytes hemostasis
- BMD management
- Dialysis adequacy
Hemodialysis Adequacy

The delivered dose of hemodialysis that will optimize the survival and well-being of the patient
Hemodialysis Adequacy

The importance of dialysis adequacy on:

✓ Mortality and survival
✓ Tools to measure adequacy
✓ Interventions to achieve adequate dialysis
Defined as the absence of clinical symptoms and signs of uremia but Symptoms and signs may have other etiology
Major symptoms and signs indicating inadequate dialysis if no other etiology could be determined

- **Gastrointestinal** and nutrition
  - Nausea, vomiting, anorexia, dysgeusia, hypoalbuminemia

- **Neurological**
  - Motor neuropathy, restless leg syndrome, burning feet syndrome, insomnia, depression, pruritus, decreased nerve conduction velocity, sleep apnea

**Cardiovascular**
- Hypertension, arrhythmia related to electrolyte disturbances, pericarditis

**Hemodialysis disequilibrium**
- Headaches during or immediately after dialysis
  - **Intradialytic** and postdialytic hypovolemia
  - **During dialysis**: cramps, hypotension, backache, crash.
  - **After dialysis**: dizziness, hangover (thirst, headache, fatigue)
Adequate dialysis now

Optimal dialysis is the dialysis service that result in improving QoL, decreasing mortality and morbidity among dialysis population.
Global dialysis population

Global
1,400,000 Patients

Rest of World
445,000 Patients
32%

Europe
346,000 Patients
25%

Japan
256,000 Patients
18%

US
353,000 Patients
25%

US
353,000 Patients ($15B)

Hemodialysis
327,000 Patients
93%

Peritoneal Dialysis
26,000 Patients
7%

7% Annual WW Growth
(5% Annual US Growth)

*USRDS Projections
Regional dialysis population

Nb: 49474

- Algeria: 20312
- Libya: 14026
- Morocco: 1220
- Mauritania: 9786
- Tunisia: 4130

pmp

- Algeria: 523
- Libya: 661
- Morocco: 425
- Mauritania: 347
- Tunisia: 895
Cardiovascular mortality in general population VS ESRD patients
Mortality in Hemodialysis Patients in Europe, Japan, and the United States
Relative Risk of Death and First Hospitalization by Quintile Scores for Physical Component Summary

Adjusted relative risk

- Physical component summary score
  - Death
  - Hospitalizations

1.93 > 25
1.52 32-26
1.56 38-33
1.46 46-39
1.33 46<
Tools to improve dialysis adequacy
Adequate dialysis evaluation

Defined as the absence of clinical symptoms and signs of uremia

but

Symptoms and signs may have other etiology

So how to evaluate adequacy
Hemodialysis Dose Measurement

- The preferred method is by formal kinetic urea modeling
- K/DOQI 2015 still ok
- HD adeq 2015.pdf
- But not alone ...2018..
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 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)

dialysis modality over the other and the possibility that conservative care may be the option that best fits some individual patients’ goals. Morton and colleagues recently provided a thematic synthesis of 18 qualitative studies that reported the experience of 375 patients and 87 caregivers. They identified 4 major themes central to treatment choices: confronting mortality (choosing life or death, being a burden, living in limbs), lack of choice (medical decision, lack of information, constraints on resources), gaining knowledge about options (peer influence, timing of information), and weighing alternatives (maintaining lifestyle, family influence, maintaining status quo). However, none of the essential decisions can be made in an informed manner without adequate time for education and contemplation.

As illustrated by Morton and colleagues’ systematic review, electing conservative therapy rather than dialysis or kidney transplantation is an important option for many people with kidney failure. In one study of 584 patients with CKD stages 4 and 5, a total of 61% of the patients who had started HD regretted this decision.39 and when asked why they chose dialysis, 52% evaluating similar HD prescriptions. Further, differences in the type of therapy, the dialysis prescription, and the patient’s preferences and the care often differ. Many patients perform HD for 3 or more times a week or more frequent sessions themselves at home, or are fully or partially assisted by technicians in an outpatient treatment facility. Blood and dialysate flow rates can differ between these treatment categories. Such discrepancies arise when different prescriptions are compared and these variables are not taken into account. For these reasons, we believe that the normative level of care should be unified.

In concordance with the KDIGO Workgroup, we suggest that all HD prescriptions consider the duration of the individual dialysis sessions, the number of treatments per week, blood and dialysate flow rates, the location for HD treatment, and the level of assistance. A proposed nomenclature is given in Table 6.

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)

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 long 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. (IB)

3.2 In patients with significant residual native kidney function (Kru), the dose of hemodialysis may be reduced provided Kru 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)

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. (ID)

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, hyperkalemia, and left ventricular hypertrophy. (IB)
Hemodialysis Dose Measurement

- **Kt/V**
  
  $K = \text{dialyzer urea clearance } \text{L/h}$
  
  $t = \text{dialysis session length } \text{hr}$
  
  $v = \text{distribution volume of urea } \text{L}$

- **URR**
Measures of dialysis adequacy

- SpKt/V
- eKt/V
- StdKt/V
- URR
Urea reduction Ratio (URR)

$$\text{URR} = \left( \frac{[\text{BUN}_{\text{pre}} - \text{BUN}_{\text{post}}]}{\text{BUN}_{\text{pre}}} \right) \times 100$$
Urea Reduction Volume (URR)

- Simple
- Prediction of mortality

Limitation:
Does not account for the contribution of UF to dialysis dose

\[
\begin{align*}
\text{URR} & = 65 \\
Kt/V & = 1.1 \ (UF=0) \\
Kt/v & = 1.35 \ (UF=10\%\text{BW})
\end{align*}
\]
URR & Kt/V

BUN Sampling

- Predialysis
- Postdialysis
- Immediate predialysis
- Slow flow/stop pump
BUN Sampling

PROVINCIAL STANDARDS & GUIDELINES

UREA TESTING
PRE & POST HEMODIALYSIS

Created: July 2015
Approved by the BC PRA Hemodialysis Committee
Urea Rebound

- Organs with low blood flow (skin, bone, muscles) may serve as reservoir for urea 70% of TBW is contained in organs that receive only 20% of CO

So: during HD, there is loss of urea from well perfused areas, this result in ↑ in BUN over 60 minutes post dialysis.
Urea Rebound

- For most patients, urea rebound is nearly complete in 15 minutes after hemodialysis but for minority, it may require up to 50-60 minutes.

- The degree of rebound is high in small patients.
Single-Pool vs Double-Pool

**Single-pool**

Does not account for urea transfer between fluid compartments. With ↑ dialyzer clearance, urea removed from extracellular compartment can exceed transfer from intracellular compartment.

Urea rebound (30-60 min)

So: Dialysis dose will be overestimated if this urea pool is large (underestimated of true V)
Kt/V

Computerized software
Mathematical logarithm

\[ Kt/v = -\ln (R-0.008t) + (4-3.5xR) \times \frac{UF}{W} \]

Ln = natural logarithm
R = postdialysis BUN
predialysis BUN
UF = Ultrafiltration volume in liters
W = Postdialysis weight in kg
Equilibrated Kt/V

- eKt/v is 0.2 units less than single-pool kt/v, but it can be as great 0.6 unit less.
  - eKt/V = spKt/V - 0.6 x (spKt/V) / t + 0.03
    - (for arterial access)
  - eKt/V = spKt/V - 0.47 x (spKt/V) / t + 0.02
    - (for venous access)
Daugirdas Formula

Calculator: Kt/V Dialysis Dose Daugirdas Formula

\[ Kt/V_{Daugirdas} = \ln\left(\frac{\text{BUN Post}}{\text{BUN Pre}}\right) - (0.008 \times \text{Hours}) + \left(\frac{(4 - (3.5 \times \text{BUN Post} / \text{BUN Pre})) \times \text{UF Vol}}{\text{Weight Post}}\right) \]

Input:
- BUN Pre: mg/dL
- BUN Post: mg/dL
- Hours: hr
- UF Vol: L
- Weight Post: kg

Result:
- Kt/V Daugirdas
- Decimal Precision: 2
Prescribed Kt/V is a computerized estimation of what the patients Kt/V would be, based on the prescription.

• Delivered Kt/V is actual results based on how the patient really dialyzed the day the kinetic labs were drawn.
Discrepancies Between Delivered and Prescribed Dialysis Dose

**Delivered less than the prescribed:**

- Low blood flow
- Inadequate dialyzer performance
- Low dialysate flow
- Dialysis machine programmed incorrectly
- Hemodialysis ended prematurely
- The predialysis BUN was drained after initiation of hemodialysis
- Access recirculation
Discrepancies Between Delivered and Prescribed Dialysis Dose

- **Delivered Dose More than the Prescribed:**
  - Postdialysis BUN was drained from venous bloodline
  - The post dialysis BUN was diluted with saline
  - Small (V)
Low \(kt/v\)

- **Kt/V below goal**
- **Kt/V low**
- **Confirm “V” value is appropriate**
- **Increase duration and or frequency of HD sessions**
- **Check QB, QD and Filter selection \(K_0A\)**
- **Check Access Recirculation**
- **Check Anticoagulation Efficiency**
- **Low \(Kt/V\)^1**
  - Low QB or \(t\) (40% of cases)
  - Access recirculation (25% of cases)
  - Other (large \(V\), blood tubing, low QD etc)

Problems fixed;
How to improve clearance

• Blood flow
• Dialysate flow
• Duration
• Frequency
• Dialyzer
Prescribed blood flow, HD duration, and percent fistula in prevalent patients in Japan, Euro-DOPPS, and the USA

Calculated from DOPPS data kindly provided by Dr. Phil Held

Blood flow (mL/min), HD Duration (min), Fistula (%)

- **Japan**
  - Blood flow: 200 mL/min
  - HD Duration: 240 min
  - Fistula: 90.2%

- **Euro-DOPPS**
  - Blood flow: 228 mL/min
  - HD Duration: 300 min
  - Fistula: 73.7%

- **USA**
  - Blood flow: 400 mL/min
  - HD Duration: 210 min
  - Fistula: 19.9%
High blood flow rates and A-V fistula problems

Primary A-V wrist fistula providing <300 mL/min blood flow is sufficient for long dialysis but is in jeopardy if short dialysis is practiced.

May be deemed unusable and other access created.
Do you know why?

A-V fistula survival is markedly higher in Europe compared to the USA.

Short dialysis x hi blood flow
High blood flow rates and A-V fistula problems

A-V fistula may be damaged by repeated attempts to achieve higher blood flows, using tourniquets and other maneuvers.

Hypotensive episodes rapidly reduce fistula blood flow, predispose to damage of the intima by suction of the inflow needle with consequent clotting.
High blood flow and catheter problems

High blood flow requires a large internal diameter of the catheter.

Large diameter catheter fits the vein too tightly and predisposes to damage of the vein wall, vein thrombosis and stenosis.
Blood flow and Clearance

- **Flow-limited** (high KoA)
- **Membrane-limited** (low KoA)
Blood flow and Clearance

![Graph showing urea clearance vs. blood flow rate for different dialyzers (KoA 900, KoA 650, KoA 300) and dialysis techniques (flow-limited, membrane-limited).]
How to improve clearance

- Blood flow
- Dialysate flow
- Duration
- Frequency
- Dialyzer
Dialysate flow and clearance
How to improve clearance

- Blood flow
- Dialysate flow
- Duration
- Frequency
- Dialyzer
The dialysis dose

Short V long dialysis

The effect on survival
Why Should We Measure Dialysis Dose?

- There is a correlation between delivered dose of hemodialysis and patient morbidity and mortality
- Clinical symptoms are not reliable
“Shortening the time of dialysis has always been an aim of physicians”.

- **Kt/V**
  
  $K =$ dialyzer urea clearance $L/h$
  
  $t =$ dialysis session length $hr$
  
  $v =$ distribution volume of urea $L$

First Randomized Controlled Trial In Dialysis

- The National Cooperative Dialysis Study (NCDS) was the first multicentric, randomized and controlled trial to investigate the impact of dialysis dose on patients' outcome. 160 patients were randomized to two different urea time-averaged concentrations (TAC; 100 vs 50 mg/dl) and to two different treatment times (2.5–3.5 vs 4.5–5.5 h) and followed-up for 6 months.

NCDS 1980
First Randomized Controlled Trial In Dialysis

Predialysis urea 38 vs 26 mmol. Dialysis 2.5-35h vs 4.5-5 h

- high kt/v and long dialysis
- high kt/v and short dialysis
- low kt/v and long dialysis
- low kt/v and short dialysis
Secondary analysis of NCDS

- A quantification of dialysis dose using spKt/V was first proposed by Gotch in a secondary analysis of NCDS data.

- In his analysis, probability of dialysis failure was higher for $Kt/V \leq 0.8$ and abruptly decreased for $Kt/V > 0.9$
NCDS Conclusion

• Thus, according to NCDS patient morbidity and treatment failure are related to the dialysis dose
Analysis of the results in 71,193 patients of Japanese HD Registry showed statistically significant, gradual decrease of mortality with increased dialysis time from 3.5 to 5.5 hours.

Further decrease in mortality with dialysis duration >6 hours, but statistically insignificant because of small number of patients in this time range.
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<tr>
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<td>90 m</td>
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How to improve clearance

- Blood flow
- Dialysate flow
- Duration
- Frequency
- Dialyzer
Importance of dialysis frequency higher than thrice weekly

Sudden and cardiac death highest on Monday and Tuesday in HD

QOD, 4, 5, 6, and 7 times weekly HD decrease fluctuations in pre and post dialysis fluid volumes and solute concentrations

Decrease interdialytic and intradialytic symptoms  IDH, cramps, and postdialysis hangover

Improve mental health, energy, social functioning, physical activity, vitality, blood pressure control with decreased use of antihypertensive drugs, and hematocrit with decreased use of erythropoietin
Reasons that patients do better on quotidian HD with the same overall weekly dialysis duration

Alleviation of hemodialysis “unphysiology”

Less swings in concentrations of all solutes (lower time average deviation)
Urea, creatinine, uric acid, etc.

Maintenance of concentrations within normal limits
Potassium, phosphorus, calcium, pH, bicarbonate

Less swings in hydration/ECV
Lower interdialytic weight gains
Elimination of hypervolemia/hypovolemia
Weekly substance concentrations in routine HD

Weekly fluctuations in routine hemodialysis

NO NORMAL RANGE OF ECV, K, Bicarb, P, Ca, pH
Weekly substance concentrations in daily HD

Weekly fluctuations in daily hemodialysis

NORMAL RANGE OF ECV, K, Bicarb, P, Ca, pH
Intradialytic hypotension (IDH) occurs in 25 to 50% of short, thrice weekly hemodialysis treatments in the United States.

Dialysis hypotension occurs because a large volume of blood water and solutes are removed over a short period, exceeding the plasma refilling rate and reduction of venous capacity.
Recommended maneuvers to decrease IDH episodes

✓ Higher dialysate sodium, calcium, and potassium
✓ Isolated ultrafiltration followed by dialysis
✓ Lower dialysate magnesium, high dialysate potassium
✓ Lower dialysate temperature
✓ Bicarbonate instead of acetate dialysate
✓ Predialysis withdrawal of blood pressure medications
✓ Blood pressure raising drugs, such as ephedrine, fludrocortisone, caffeine, and midodrine
✓ Sodium and ultrafiltration modeling (profiling)
## TABLE 2. Continued

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<th>Reference</th>
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<th>From</th>
<th>To</th>
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Exchangeable sodium increases with 14.8 hr/wk compared to 18 hr/wk dialysis, and more patients require antihypertensive drugs.

Problems of hypertension and the side effects of its treatment, both medical and surgical, should be weighed against the social and economic advantages of short dialysis in deciding on the ideal schedule.”
Consequences of positive sodium balance

Chronic fluid volume overload until new equilibrium is achieved

Decreases IDH rates

Causes volume dependent hypertension
  >80% of patients in the USA are on antihypertensive drugs
  LVH
  Increased cardiovascular mortality
## Comorbidities (%) in Euro- DOPPS, Japan, and the USA

<table>
<thead>
<tr>
<th>Condition</th>
<th>Euro-DOPPS</th>
<th>Japan</th>
<th>USA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary artery disease</td>
<td>28.7</td>
<td>18.7</td>
<td>48.3</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>24.1</td>
<td>5.6</td>
<td>43.9</td>
</tr>
<tr>
<td>Other cardiac problem</td>
<td>36.2</td>
<td>23.9</td>
<td>34.6</td>
</tr>
<tr>
<td>Hypertension</td>
<td>72.5</td>
<td>56.1</td>
<td>83.7</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>22.0</td>
<td>10.9</td>
<td>24.3</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>13.2</td>
<td>11.8</td>
<td>16.8</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>18.9</td>
<td>2.4</td>
<td>27.5</td>
</tr>
</tbody>
</table>
Higher Kt/V has better outcome

PF2 = 0.57

Kt/V = 1.2
Increasing dialysis dose improved survival
Conclusion of NCDS

Time of dialysis has little influence on results provided that dialyzer clearance is high.

\[ Kt/V_{urea} \text{ should be over } 0.95/\text{treatment with three times weekly dialysis} \]
Call for change of paradigm

Time and frequency of dialysis must be adjusted to residual urine output and tolerance of ultrafiltration. Ultrafiltration rate should range from 0.5%-1.5% of body weight/hr.

Dialysis frequency and duration should permit the achievement of blood pressure control without antihypertensive medications in 90%-95% of patients.

Anuric patients should not have dialysis shorter than five hours in thrice weekly schedule.

More frequent dialysis is preferred in anuric patients, but weekly dialysis time should not drop below 15 hrs.
Call for change of paradigm

➢ Kt/V , URR should be measured max every 8 wks to 2 months to evaluate dialysis quality
➢ URR ≥ 70  Kt/V 1.4 is accepted for adequacy
➢ Blood flow should range from 200 to 300 ml/min
➢ Dialysate flow to be 500 ml / min
➢ High performance dialyzers should continue to be used
➢ Management of comorbid conditions to be planned
➢ Quality of life to be routinely assessed
Better survival with long dialysis
How to improve clearance

- Blood flow
- Dialysate flow
- Duration
- Frequency
- Dialyzer
Efficiency and Flux

- **Efficiency**: ability to achieve large small solute clearance with high blood flows (all filters are high efficiency these days)
- **Flux**: ability to achieve high middle molecule clearance and ultrafiltration rate (determined by the average pore size)

Diffusion and Convection

- **Diffusion**: solutes move by diffusion between blocks of fluid separated by the membrane
- **Convection**: solutes move en mass with a block of fluid across the membrane (more effective for moving large molecules)